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JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY

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MORTIMER D. SACKLER, M.D.

Editors in Chief

The van Ophuijsen Center, New York, N. Y.

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*Professor and Director of the Department of the History of Medicine,
New York Medical College, Flower and Fifth Avenue Hospitals;
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a new perspective in the study of disease ecology

THE ECOLOGY OF HUMAN DISEASE



by

JACQUES M. MAY, M.D.

Director, Medical Geography Department,
American Geographical Society, New York

foreword by

FELIX MARTI-IBAÑEZ, M.D.

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About the Author: Dr. Jacques M. May is head of the Medical Geography Department of the American Geographical Society in New York, where he has been engaged since 1948 in compiling the *Atlas of Diseases*, which comprises in the form of maps as comprehensive a presentation of the distribution of certain human diseases as available data will permit. Dr. May is a member of the staff of the Medical School of New York University in the field of preventive medicine and a visiting lecturer at the School of Tropical Medicine of Harvard University and at the School of Public Health of Columbia University.

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Assistant Professor of Clinical Neurology and Psychiatry;

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JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY

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Clinical Psychopathologic Conferences are often included as a feature of the JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY. This section will attempt to further the elucidation of correlations and associations between clinical, neurologic, psychologic, and biologic elements. Clinical case presentations illustrative of psychophysiopathologic disorders will be gathered from psychiatric hospitals, clinics, and psychiatrists throughout the world. Manuscripts together with accompanying illustrations should be forwarded to the JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY, 30 East 60th Street, New York, N. Y., Attention: Editor, Clinical Psychopathologic Conferences.

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JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY & QUARTERLY REVIEW OF PSYCHIATRY AND NEUROLOGY

— * —

Hematologic Studies on Psychotic Patients Under Chlorpromazine Medication*

F. CoTui, E. Riley, H. Tazaki, L. Goldschmidt, and L. Hicks

QUEENS VILLAGE, NEW YORK

The frequent occurrence of a fall in the hemoglobin level and the erythrocyte count during chlorpromazine therapy as early as the first two weeks of administration raises the question whether this fall represents anemia or some other factor. In psychotic patients in whom emotional or physiological instability may affect fluid intake, leading to changes in hydration, an expansion of the plasma volume could well be one factor. The administration of a drug that tends to restore stability would be expected to reverse these effects in both the plasma volume and the blood picture.

It is well known that the hematologic values in common use—hemoglobin value, erythrocyte count, and venous hematocrit—merely represent the levels in the circulation and not total quantities. To arrive at total quantities, it is necessary to determine the plasma

From Creedmoor Institute for Psychobiologic Studies and the Creedmoor State Hospital, Queens Village, N. Y. The assistance of Mrs. Evelyn Davis, Mrs. Eleanore Alesi, and Mr. Rosario Niosi is gratefully acknowledged.

* The trade name of Smith, Kline & French, Philadelphia, for chlorpromazine hydrochloride is Thorazine.

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volume. From the plasma volume and the venous hematocrit is derived the blood volume. The difference between the blood volume and the plasma volume gives the total red cell mass, and from the blood volume and the hemoglobin level is determined the total circulating hemoglobin. In this paper, the hemoglobin value, erythrocyte count, and venous hematocrit will be termed the indices.

The present investigation was primarily directed at the changes in the total red cell mass during chlorpromazine medication. However, since serial studies were involved and since there were no available data on the changes in the blood compartments and blood elements serially from week to week in psychotics, it seemed desirable to undertake the study of these changes also as a base line.

MATERIALS AND METHODS

Altogether, 17 male patients were used in the study, ranging in ages from 23 to 47 years and in hospital residence from 19 months to 21 years and 10 months. All were without detectable somatic disease and, with two exceptions, carried the diagnosis of schizophrenic reaction.

In part I of the study, 9 of these patients were subjected to serial determinations of body weight, hemoglobin value, erythrocyte count, venous hematocrit, and plasma volume at weekly intervals for two weeks in 3 patients, three weeks in 4 patients, and four weeks in 2 patients. From the plasma volume (PV) and the hematocrit (Hct) was derived the blood volume (BV) according to this formula:¹

$$BV = \frac{PV \times 100}{Hct \times 0.92' \times 0.91'}$$

The total red cell mass was obtained as the difference between the blood volume and the plasma volume.

The hemoglobin value was determined by the acid hematin method using the Sahli-Haden hemoglobinometer,² the erythrocyte count on the Spencer bright-line counting chamber, the venous hematocrit by use of the Wintrobe tube, and the plasma volume by the 1824 dye method of Gregersen.³

Part II consisted of a study by similar methods on patients under chlorpromazine medication. Of the 15 patients in this series, 7 were from part I; their medication was started after the control serial studies had ended. The additional 8 patients, also men, had only one battery of premedication tests.

RESULTS

The results in both series appear in table I, with values for parts I and II indicated for each patient.

Part I. Since the blood constituents and compartments are affected by changes in body weight,⁵ tests in patients in whom there was a change of ± 2 per cent of the initial body

HEMATOLOGIC STUDIES AND CHLORPROMAZINE

weight were discarded. The initial hemoglobin values were all within normal limits; the initial erythrocyte values were also within normal limits except in patient S-1 whose erythrocyte count was slightly under normal. Patients S-1 and D had hematocrit values under normal.

In subsequent determinations, it is seen from the table that the largest changes in hemoglobin were +11.1 and -10 per cent (patients L and G); in erythrocyte +25.8 and -20.7 per cent (patients A and G); and in hematocrit +8.6 and -6.5 per cent (patients N-1 and G); in plasma volume +4.9 and -8.9 per cent (patients D and G); in blood volume +5.3 and -10.1 (patients S-1 and G); and in total red cell mass +10.1 and -14.3 per cent (patients S-1 and G). It is clear that the stability of values are in this order: hematocrit, hemoglobin, plasma volume, blood volume, total red cell mass, and, last, erythrocyte count. From this study, it would appear that all these values, by and large, are held within narrow limits in psychotic patients whose weight does not change more than ± 2 per cent.

In the 7 patients from part I, the last set of premedication values was considered the initial set from which all the percentage changes during the period of medication were determined.

In view of the findings in part I, the allowable variations of hemoglobin from the initial values of the patients in Part II may be set at ± 10 per cent, of hematocrit ± 8 per cent, of plasma volume ± 12 per cent, of blood volume ± 20 per cent, and of total red cell mass ± 20 per cent. The limits of erythrocyte count, according to this study, should be set at ± 25 , higher than the range allowed in the literature.⁴ However, this erythrocyte value is merely of incidental importance in the present work and is included only for the purpose of showing how faithfully it reflects the total red cell mass.

The indices were all within normal limits in the 8 additional patients in part II except for patient S-3, who had a 12 Gm. initial hemoglobin value.

Part II. CHANGES AFTER ONE WEEK OF CHLORPROMAZINE. Seven patients were available for the battery of tests after one week of chlorpromazine medication. They were patients S-1, S-2, S-3, P-1, P-2, H-3, and N-1. With ± 2 per cent weight change arbitrarily chosen as significant, the body weight was found to be increased in 2 patients (N-1 and P-1), was unchanged in 3 (P-2, S-2, and S-3), and decreased in 2 (S-1 and H-3).

The hemoglobin, erythrocyte count, and hematocrit fluctuated within narrow limits except for a fall in hematocrit in patient L. The plasma volume, however, showed definite expansion in 4 patients (S-3, N-1, S-2, and P-2) and a fall in only 1 (P-1). The blood volume followed the trend of plasma volume in all instances, and the total red cell mass showed a fall only in patients P-1 and H-3, the fall in H-3 probably being significant, but remained unchanged in the other five.

The notable change in the first week, then, may be said to be expansion of the plasma volume in more than half the subjects and a slight tendency of the total red cell mass to fall. That the dosage of the drug had little direct bearing on the magnitude of these changes is shown in the fact that P-2, who was taking 1.75 Gm. daily during this period, had changes of similar magnitude to those of N-1 and S-2 whose dosages were respectively 7.2 and 8.4 Gm. in the same period.

TABLE I
Serial Blood Studies on Psychotic Patients

Pt., age, diagnosis	Date, 1955	Ht., cm.	Wt., Kg.	Wt.		Hemoglobin		Erythrocyte		Hematocrit	
				% change	Gm. % change	% change	× 10 ⁶ change	Venous	Corr.	% change	
Part I											
D, 27,	6/15	154	61.82	—	13.5	—	4.2	—	46.8	39.18	—
schiz- paranoid	6/22	—	61.82	—	14	+3.7	4.5	+7.1	45.8	38.18	-2.1
Part I											
H-1, 29,	6/15	145	80	—	14.5	—	4.85	—	45.5	38.09	—
schiz- paranoid	6/22	—	78.64	-1.7	14.5	—	4.84	-0.2	45.8	38.34	+0.7
Part I											
S-1, 23,	2/16	166	87.27	—	11.5	—	3.93	—	49.5	41.69	—
psychosis	2/23	—	88.18	+1	11.5	—	4.02	+2.3	52.2	43.7	+5.4
Part II											
3/2	—	84.09	-4.6	11	-4.3	3.59	-10.7	51.8	43.37	-0.77	
3/16	—	84.54	-4.1	12	+4.3	3.87	-3.7	45.6	38.18	-12.6	
4/20	—	86.36	-2.1	13	+13	—	-1.5	46.7	39.10	-10.5	
Part I											
S-2, 33,	4/20	158	94.54	—	14	—	4.8	—	53.4	—	—
schiz- paranoid	4/27	—	95.45	+1	14	0	4.72	-1.7	52	43.53	-2.6
Part II											
5/4	—	95.45	0	13	-7.1	4.44	-5.9	47.8	40.02	-8.1	
5/11	—	93.64	-1.9	13.5	-3.6	4.65	-1.5	52.4	43.87	+0.77	
Part I											
N-1, 33,	4/13	150	59.68	—	15	—	5.4	—	46.5	38.93	—
schiz- catatonic	4/20	—	59.55	-0.2	15	0	—	0	50.5	42.28	+8.6
4/27	—	59.09	-1.0	15	0	5.2	-3.7	45.2	37.84	-2.8	
Part II											
5/4	—	60.91	+3.1	13	-13.3	4.5	-13.5	39.2	32.82	-13.3	
5/11	—	60	+1.5	13	-13.3	3.96	-23.8	42.3	36.25	-6.4	
5/18	—	61.36	+3.8	12	-20	4.04	-22.3	41.3	34.58	-8.6	
6/1	—	68.54	+16.0	14.5	-3.3	5.00	-3.8	43.1	36.08	-4.6	

TABLE I
Before and During Chlorpromazine Medication

% change	Plasma volume		Blood volume		Total red cell mass		Remarks; total cumulative dosage (TCD)
	L.	% change	L.	% change	L.	% change	
2.1	2.46	—	4.04	—	1.58	—	Admitted Sept., 1951. Up and about, cooperative, emotionally bland, somatic and religious delusions, grandiose ideas, mild paranoid trends, sensorium intact. No medication.
2.1	2.58	+4.9	4.17	+3.2	1.59	+0.6	
0.7	2.92	—	5.94	—	2.26	—	Admitted Feb., 1944. Up and about, eats and sleeps well, clean habits, assaultive without provocation, emotionally blunted, consistently mute, obeys simple commands. EEG, moderate slow activity. No medication.
0.7	2.86	-2.1	6.01	+1.17	2.3	+1.8	
4	3.32	—	5.68	—	2.37	—	Admitted March, 1949. Psychosis with mental deficiency, up and about, withdrawn, inadequate, emotionally blunted, relevant, denies delusions and hallucinations, memory poor.
4	3.37	+1.5	5.98	+5.3	2.61	+10.1	
5	3.19	-5.3	5.63	-5.9	2.44	-6.5	Medication started 2/28. TCD 8.4 Gm. by 3/2. Dizzy, weak, ashen. 3/16 medication discontinued.
5	3.15	-6.5	5.12	-14.4	1.97	-24.5	TCD 31.2 Gm. by 3/16. Medication resumed 3/18. TCD 42.2 Gm. by 4/20.
6	4.5	—	8.13	—	3.63	—	Admitted Nov., 1952. Up and about, quiet, cooperative, idle, relevant, suspicious and evasive, memory poor, sensorium intact, paranoid trends, threatening legal action.
6	4.26	-5.3	7.54	-7.3	3.28	-9.6	
7	5.18	+21.6	8.63	+14.5	3.45	+5.1	Medication started 4/28. TCD 7.2 Gm. by 5/4. TCD 26.2 Gm. by 5/11.
7	3.96	-7	7.05	-6.5	3.09	-5.7	
2.7	2.76	—	4.51	—	1.75	—	Admitted Sept., 1941. Up and about, self-absorbed, assaultive, regressed, incoherent, hallucinating.
2.7	2.42	-12.3	4.19	-7.1	1.77	+1.1	
2.7	2.7	-2.2	4.34	-3.8	1.64	-6.3	
3.48	3.50	+29.6	5.2	+19.8	1.7	+3.7	Medication started 4/28. TCD 8.4 Gm. by 5/4, 16.8 Gm. by 5/11, 33.6 Gm. by 5/18, 69.6 Gm. by 6/1.
3.08	3.48	+28.9	5.45	+25.6	1.87	+14	
3.10	3.08	+14.1	4.7	+8.3	1.62	-1.2	
3.10	3.10	+14.8	4.84	+11.5	1.74	+6.1	

Table I Continued on Page 114

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TABLE I (Continued)
Serial Blood Studies on Psychotic Patients

Pt., age, diagnosis	Date, 1955	Ht., cm.	Wt., Kg.	Wt.		Hemoglobin		Erythrocyte		Hematocrit	
				% change	Gm. %	% change	× 10 ⁶	% change	Venous	Corr.	% change
Part I											
A, 35, schiz- catatonic	6/1	143	73.64	—	14	—	4.5	—	52	43.53	—
	6/8	—	72.63	+1.4	14	0	4.46	-0.8	53.7	44.96	+3.3
	6/15	—	73.18	-0.6	15.5	+10.7	5.66	+25.8	52.8	44.2	+1.5
Part II											
	6/29	—	69.9	-4.5	15	-3.2	5.45	-3.7	50.9	42.61	-3.6
Part I											
G, 45, schiz- hebe- phrenic	5/4	155	76.36	—	15	—	5.8	—	50.5	42.28	—
	5/11	—	76.36	0	13.5	-10	4.7	-19	48.2	40.35	-4.6
	5/18	—	76.36	0	14	-6.6	4.83	-16.7	47.5	39.77	-5.9
	5/25	—	77.26	+1.2	13.5	-10	4.6	-20.7	47.2	39.52	-6.5
Part II											
	6/8	—	77.73	+0.6	14.5	+7.4	5.10	+10.9	47.4	39.68	+0.4
	6/22	—	77.73	+0.6	14.5	+7.4	4.84	+5.2	43.9	36.75	-7
Part I											
L, 42, schiz- paranoid	5/4	138	68.18	—	13.5	—	4.7	—	51	42.7	—
	5/11	—	68.18	0	15	+11.1	5.4	+14.9	53.5	44.79	+4.9
	5/18	—	67.73	-0.7	15	+11.1	5.35	+13.8	50.5	42.28	-1
Part II											
	6/8	—	68.18	+0.7	14	-6.7	4.31	-19.4	46.3	38.76	-8.3
	6/22	—	69.09	+2	14	-6.7	4.50	-15.9	43.9	36.75	-13.1
Part I											
H-2, 36, psychosis with alcohol- ism	5/18	156	71.82	—	15	—	4.93	—	52.2	43.7	—
	5/25	—	72.73	+1.3	14	-6.7	4.5	-8.7	50.1	41.9	-4
	6/1	—	72.28	+0.6	13.5	-10	4.35	-11.8	53	44.37	+1.5
	6/8	—	70.91	-1.3	14	-6.7	4.6	-6.7	54.5	45.63	+4.4
Part II											
	6/29	—	72.72	+2.6	14	0	4.62	+0.4	49.7	41.61	-8.8
Part I											
P-1, 36, schiz- catatonic	3/23	154	67.73	—	14	—	4.83	—	47	39.35	—
Part II											
	3/30	—	70	+3.4	14.5	+3.6	5	+3.5	45	37.67	-4.3
	4/6	—	66.4	-2	15	+7.1	5.5	+13.9	45.2	37.84	-3.8
	4/13	—	66.4	-2	15	+7.1	5.8	+20.1	46.2	38.68	-1.7
	5/18	—	70	+3.4	14.5	+3.6	5.03	+4.1	46.4	38.85	-1.3
	6/29	—	70	+3.4	14.5	+3.6	5	+3.5	45.7	38.26	+2.8

TABLE I (Continued)
Before and During Chlorpromazine Medication

Plasma volume		Blood volume		Total red cell mass		Remarks; total cumulative dosage (TCD)
L.	% change	L.	% change	L.	% change	
2.76	—	4.88	—	2.12	—	Admitted Dec., 1954. Up and about, cooperative, occasionally tense, speech disconnected, mild paranoid trends.
2.67	-3.3	4.85	-0.6	2.18	+2.8	
2.75	-0.4	4.92	+0.8	2.17	+2.4	
3.05	+10.9	5.31	+7.9	2.26	+4.1	Medication started 6/16. TCD 3.9 Gm. by 6/29.
3.16	—	5.47	—	2.31	—	Admitted Jan., 1958. Up and about, seclusive, idle, eats poorly, silly, inappropriate mannerisms, incoherent, auditory hallucinations, mild paranoid ideas, well orientated.
2.94	-7.	4.92	-10.1	1.98	-14.3	
3.25	+2.8	5.39	-1.46	2.14	-7.4	
3.37	+6.6	5.57	+1.8	2.20	-4.8	
3.07	-8.9	5.08	-8.8	2.01	-8.6	Medication started 5/26. TCD 10.4 Gm. by 6/8,
3.37	0	5.32	-4.5	1.95	-11.4	44 Gm. by 6/22.
3.14	—	5.47	—	2.33	—	Admitted April, 1953. Up and about (works in kitchen), seclusive, in poor contact, depressed, confused, hesitant speech, evasive to questions, denies hallucinations (thyroidectomy 1952).
2.86	-8.9	5.18	-5.3	2.37	+1.7	
2.95	-6.1	5.11	-6.6	2.16	-7.3	
3.11	+5.4	5.07	-0.8	1.96	-9.2	Medication started 5/26. TCD 10.4 Gm by 6/8,
3.42	+15.9	5.4	+5.6	1.98	-8.3	44 Gm. by 6/22.
3.43	—	6.09	—	2.66	—	Admitted May, 1953. Up and about, quiet, complacent, denies all abnormal ideas, emotionally bland, resentful of confinement, unable to understand why hospitalized.
3.28	-4.4	5.85	-3.9	2.57	-3.4	
3.30	-3.8	5.93	-2.6	2.62	-1.5	
3.17	-7.6	5.83	-4.3	2.66	0	
3.56	+12.3	6.09	+4.5	2.53	-4.9	Medication started 6/9. TCD 35.2 Gm. by 6/29.
3.56	—	5.87	—	2.31	—	Admitted June, 1942. Up and about, confused, impulsively assaultive, completely out of contact, rambling incoherently, responding to hallucinations.
3.08	-13.5	4.94	-15.8	1.86	-19.5	Medication started 3/23. TCD 8.4 Gm. by 3/30,
2.77	-22.2	4.45	-24.2	1.68	-27.3	16.8 Gm. by 4/6, 25 Gm. by 4/13, 74.11 Gm. by
3.52	-1.1	5.74	-2.2	2.22	-3.9	5/18, 107.71 Gm. by 6/29.
3.42	-3.9	5.59	-4.8	2.17	-6.1	
3.89	+9.3	6.3	+7.3	2.42	+4.8	

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TABLE I (Continued)
Serial Blood Studies on Psychotic Patients

Pt., age, diagnosis	Date, 1955	Ht., cm.	Wt.		Hemoglobin		Erythrocyte		Hematocrit		
			Kg.	% change	Gm. % change	% change	× 10 ⁶	% change	Venous	Corr.	% change
Part I											
H-3, 32, schiz- hebe- phrenic	3/16	149.6	76.36	—	12.5	—	4.34	—	51.4	43.03	—
Part II											
	3/30	—	67.27	-11.9	14.5	+16	5.1	+17.5	48.5	40.6	-5.6
	4/6	—	70	-8.3	13	+4	4.2	-3.2	47.7	39.93	-7.2
	4/13	—	68.18	-10.7	14.5	+16	5.01	+15.4	49.5	41.44	-3.7
	5/11	—	69.09	-9.5	14.5	+16	5.01	+15.4	45.8	38.34	-10.9
	6/29	—	70.45	-7.7	14.5	+16	4.85	+11.8	45.5	38.09	-11.5
Part I											
K-2, 29, schiz- hebe- phrenic	1/26	130.8	61.82	—	12.5	—	4.38	—	44.5	37.26	—
Part II											
	2/15	—	60.91	-1.5	12	-4	4.4	+0.5	40.8	34.15	-8.3
	3/2	—	61.82	0	11.5	-8	3.96	-9.6	46.8	39.18	+5.2
	3/30	—	66.36	+7.3	13	+4	4.58	+4.6	43.8	36.67	-1.6
	4/27	—	70	+13.2	11.5	-8	3.85	-12.1	44.7	37.42	+0.4
Part I											
K-1, 53, schiz- paranoid	1/12	156.2	85.45	—	15	—	5.17	—	63.3	53.00	—
Part II											
	1/26	—	85.45	0	13.5	-10	4.47	-13.5	48.2	40.35	-23.8
	2/2	—	84.54	-1.1	13.5	-10	4.56	-11.8	53.8	45.06	-15
Part I											
M, 44, schiz- catatonic	1/26	149.6	67.73	—	13.5	—	4.6	—	51.8	43.37	—
Part II											
	2/9	—	66.35	-2	11.5	-14.8	3.69	-19.8	48.1	40.27	-7.1
	3/2	—	67.68	-0.1	12.5	-7.4	4.34	-5.7	49.7	41.61	-4.1
	3/16	—	65.91	-2.7	12.5	-7.4	4.33	-5.9	45.8	38.34	-11.6
	3/30	—	67.73	0	14	+3.7	4.9	+6.5	50.5	42.28	-2.5
	4/27	—	67.68	-0.07	12.5	-7.4	4.2	-8.7	48.2	40.35	-6.9

TABLE I (Continued)
Before and During Chlorpromazine Medication

Plasma volume		Blood volume		Total red cell mass		Remarks; total cumulative dosage (TCD)
L.	% change	L.	% change	L.	% change	
2.56	—	4.99	—	1.93	—	Admitted July, 1941. Assaultive, regressed, confused laughing to self, auditory hallucinations, incoherent, mentally overactive, almost inaccessible.
2.45	-4.3	4.12	-17.4	1.67	-13.5	Medication started 3/23. TCD 8.4 Gm. by 3/30,
2.42	-5.5	4.02	-19.4	1.60	-17.1	16.8 Gm. by 4/6, 25.2 Gm. by 4/13, 57.6 Gm. by
3.11	+21.5	5.32	+6.6	2.21	+14.5	5/11, 116.4 Gm. by 6/29.
2.86	+11.7	4.63	-7.2	1.77	-8.3	
3.11	+21.5	5.03	+0.8	1.92	-0.5	
3.36	—	5.35	—	1.99	—	Admitted March, 1944. Extremely regressed, incoherent, assaultive, requiring occasional restraint.
2.91	-13.4	4.41	-17.6	1.50	-24.6	Medication started 2/2. TCD 2.1 Gm. by 2/15,
2.70	-19.7	4.43	-17.2	1.73	-13.1	16.5 Gm. by 3/2, 46.8 Gm. by 3/30, 80.4 Gm.
2.61	-22.3	4.12	-23.	1.51	-24.1	by 4/27.
3.15	-6.3	5.03	-6.	1.88	-5.5	
3.55	—	7.55	—	4.00	—	Admitted Aug., 1935. Overactive, assaultive, confused, laughing to self, rambling incoherently, auditory hallucinations, paranoid trends.
3.89	+9.6	6.52	-13.6	2.63	-34.2	Medication started 1/14. TCD 3 Gm. by 1/26.
3.54	-0.3	6.44	-14.7	2.90	-27.5	Ashen, weak. TCD 4.75 Gm. by 2/2.
2.65	—	4.68	—	2.03	—	Admitted March, 1929. Seclusive, idle, unpredictable, impulsively assaultive, incoherent, unintelligible, inaccessible.
2.67	+0.8	4.47	-4.5	1.80	-11.3	Medication started 2/2. TCD 4.2 Gm. by 2/9, 16.8
2.26	-14.7	3.87	-17.3	1.61	-20.9	Gm. by 3/2. 3/16 ashen, dizzy, weak. Drug discontinued 3/22. TCD 29.4 Gm. by 3/22. Post medication values given for 3/30 and 4/27.
2.78	+4.9	4.5	-3.8	1.72	-15.3	
2.25	-15.1	3.89	-16.9	1.64	-19.2	
2.75	+3.8	4.61	-1.5	1.86	-8.4	

Table I Continued on Page 118

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TABLE I (Continued)
Serial Blood Studies on Psychotic Patients

Pt., age, diagnosis	Date, 1955	Ht., cm.	Wt.		Hemoglobin		Erythrocyte		Hematocrit		
			Kg.	% change	Gm. % change	% change	× 10 ⁶	% change	Venous	Corr.	% change
<i>Part I</i>											
N-2, 39, schiz- paranoid	2/9	147.4	58.64	—	13.5	—	4.4	—	55	46.05	—
<i>Part II</i>											
	2/23	—	57.32	-2.3	13	-3.7	4.59	+4.3	46.8	39.18	-14.9
	3/16	—	57.32	-2.3	12	-11.1	4.1	-6.8	43.6	36.5	-20.7
	4/6	—	63.64	+8.5	12.5	-7.4	—	—	42.8	35.83	-22.2
	5/25	—	63.64	+8.5	13.5	0	4.7	+6.8	43	36.00	-21.8
<i>Part I</i>											
P-2, 47, schiz- catatonic	12/9	175	92.78	—	15	—	5.53	—	55	46.05	—
<i>Part II</i>											
	12/15	—	92.78	0	14.5	-3.3	5.44	-1.6	54	45.21	-1.8
	1/19	—	96.82	+4.4	14.5	-3.3	5.25	-5.1	53.3	44.62	-3
	3/23	—	97.27	+4.8	14.5	-3.3	5.11	-7.6	48.7	40.77	-11.5
<i>Part I</i>											
S-3, 25, schiz- paranoid	3/8	154	71.8	—	12	—	4.16	—	47.2	39.52	—
<i>Part II</i>											
	3/16	—	72.73	+1.3	11.5	-4.2	3.93	-5.5	42	35.16	-11
	3/23	—	71.8	0	11.5	-4.2	3.96	-4.8	43.3	36.25	-8.3
	3/30	—	73.64	+2.6	11	-8.3	3.89	-6.5	42.5	40.6	-10
	4/27	—	72.73	+1.3	11.5	-4.2	3.9	-6.2	45.2	37.84	-4.2

THE SECOND WEEK. Twelve patients (K-2, K-1, A, S-3, G, L, N-2, S-2, N-1, H-3, P-1, and S-1) were available for the two week tests. As in the first week, the weight changes were inconsistent, remaining relatively constant in 6 patients (K-2, K-1, S-3, G, S-2, and N-1) and registering falls in 6 (A, M, N-2, H-3, P-1, and S-1), the highest fall of -8.3 per cent being scored by patient H-3, which, however, was a gain over the larger fall of -11.9 per cent of the first week. Only L had shown a gain.

The changes in the indices were not remarkable. The plasma volume stayed within +10

TABLE I (Continued)

Before and During Chlorpromazine Medication

L.	Plasma volume		Blood volume		Total red cell mass		Remarks; total cumulative dosage (TCD)
	% change	L.	% change	L.	% change		
2.31	—	4.28	—	1.97	—	Admitted Dec. 1948. Deteriorated, untidy, mute, fearful, hallucinating, unapproachable, being spoon-fed, circulatory stasis hands and feet, fetal posture.	
2.35	+1.7	3.8	-11.2	1.45	-26.4	Medication started 2/9. TCD 19.6 Gm. by 2/23.	
2.25	-2.6	3.54	-17.3	1.29	-34.5	Dizzy, ashen, weak on arising, collapsed 3/8.	
2.07	-10.4	3.22	-24.8	1.15	-41.6	Medication discontinued 3/8. TCD 50.8 Gm. by 3/8. Postmedication value given for 3/16 (1 week post medication).	
2.85	+23.4	4.45	+40	1.60	-18.7	Medication resumed 3/18, discontinued 4/6. Postmedication value given for 5/25 (7 weeks post medication).	
2.9	—	5.39	—	2.47	—	Admitted March, 1937. Dangerous, assaultive, impulsive, in restraint 18 years, actively hallucinating.	
3.34	+15.2	6.09	+13.	2.75	+11.3	Medication started 12/9. TCD 1.8 Gm. by 12/15,	
3.22	+14.8	5.81	+7.8	2.60	+5.2	6.9 Gm. by 1/19, 37.7 Gm. by 3/23.	
2.85	-1.7	4.81	-10.6	1.96	-20.6		
2.99	—	4.94	—	1.95	—	Admitted Oct., 1949. Up and about, emotionally dull, resentful, paranoid, somatic delusions, grandiose ideas.	
3.73	+24.7	5.75	+16.4	2.02	+3.6	Medication started 3/9. TCD 1.75 Gm. by 3/16, 9.15	
3.27	+9.4	5.12	+3.6	1.85	-5.1	Gm. by 3/23, 17.55 Gm. by 3/30, 52.11 Gm. by	
2.71	-9.4	4.56	-7.7	1.85	-5.1	4/27.	
3.39	+13.4	5.46	+10.5	2.07	+6.2		

per cent in 8 patients (K-1, S-2, G, N-2, S-3, H-3, P-1, and S-1), rose above 10 per cent in 3 (A, L, and N-1), and fell below -10 per cent in only 1 (K-2). However, of those subjects who had first week values for comparison, the plasma volume of S-1 and H-2 remained practically the same as the first week. P-1 and S-2 underwent drops, and the expanded plasma volume of S-3 had dropped.

The blood volume remained within ± 20 per cent of the initial values in 7 patients (A, M, S-3, G, L, H-3, and S-2). The low normal value of -19.4 per cent in H-3 was very

close to criterion. In comparison with first week values, S-2 and S-3 had drops, whereas N-1 had a rise of nearly 25.6 per cent. It fell further in S-1 and S-2. The total red cell mass remained within 20 per cent of initial in 8 (K-1, A, M, G, L, H-3, S-2, and S-3), rose above 20 per cent in only 1 (N-1) and fell below 20 per cent in 4 (K-2, N-2, P-1, and S-1). The total red cell mass values of K-1 and K-2 respectively, -34.2 and -24.6 per cent, were significant. The fall of the total red cell mass in K-1 was reflected in a fall of 10 per cent in hemoglobin, of 13.5 per cent in erythrocyte count, and of 23.8 per cent in hematocrit. N-2, P-1, and S-1 had total red cell mass falls of fairly large magnitude, being -26.4, -27.3, and -24.5 per cent respectively, with no reflection in the indices except in N-2 and S-1, in whom the hematocrit had falls of -14.9 and -12.6 per cent of the initial values. N-1 is remarkable in being the only subject with a definite rise in total red cell mass after two weeks of medication on a total dosage of 16.8 Gm. Six of these patients had first week readings for comparison, and of these 6 the total red cell mass of only H-2 remained relatively unchanged. All the other 5 showed drops below the first week values.

As in the first week, the weight changes had no fixed pattern, remaining within 2 per cent of initial values in 6 (K-2, K-1, S-3, G, S-2, L), rising in 1 (N-1), and falling by 2 per cent or over in the other 6, with H-3 having a weight of -8.3 per cent, but actually a slight rise over the weight of the first week. Only P-1 showed a change of from +3.4 to -2 per cent. The others remained relatively stable.

Of the 4 subjects with large drops in total red cell mass, only 2 (N-2 and S-1) had marked dizziness, weakness, and pallor. These were so severe in S-1 that the dose had to be reduced from 800 to 500 mg. three times a day.

Another side reaction in a second week patient was an extensive rash on S-2, whose blood parameters, however, showed no notable changes.

THE THIRD WEEK. There were 7 patients in this period (K-1, S-3, P-1, H-3, H-2, N-1, S-1). Five of these (P-1, H-3, N-1, S-3, and S-1) had tests in both the first and second weeks. K-1 had only initial and second week tests, and H-2 had only initial tests.

H-3, on 30.5 Gm. of the ataraxic in three weeks, showed no important change apart from an expansion of the plasma volume of 21.5 per cent; S-3 showed no change from the second week. H-3, who had a drop in total red cell mass of 13.5 per cent the first week and 17.1 per cent the second, now showed a rise of 14.5 per cent, adding algebraically to a rise of over 30 per cent over the second week. P-1, who registered a fall of 19.5 per cent in the total red cell mass the first week and 27.3 per cent the second, now showed a total red cell mass of only -3.9 per cent, thus scoring a rise of some 24 per cent over the second week. S-1, whose symptoms necessitated a reduction of dosage the second week, now showed in later weeks a total red cell mass of only -8 per cent, scoring a rise of 16.5 per cent over the second week, with the symptoms of weakness and dizziness ameliorated. K-1, who showed a fall of -16.8 per cent of initial value the second week on 3 Gm. of the drug, reflected in falls of 10, 13.5, and 23.8 per cent respectively in hemoglobin, erythrocyte count, and hematocrit, showed in the third week on a total dose of 4.75 Gm. a fall of 27.5 per cent, without corresponding changes in the hemoglobin and erythrocyte count, but with the hematocrit rising from -23.8 to -15 per cent. Seeing that the plasma volume, which in

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the second week had expanded by 9.6 per cent, had practically returned to initial value in the third, this change in the hematocrit was to be expected.

The third week's events, then, seemed to be characterized by a tendency to recovery in those subjects in whom the total red cell mass had been adversely affected.

THE FOURTH WEEK. In the fourth week, only 4 patients were tested: K-2, M, G, and L. L, on 44 Gm. in four weeks, showed falls in hemoglobin, erythrocyte, and hematocrit, which were probably due to expansion of plasma volume to 15.9 per cent above initial values, a substantiation of the findings of the second week, but with relatively unchanged total red cell mass in both this and the second period. G, who showed a suggestive fall in plasma volume, blood volume, and total red cell mass the second week, now showed a plasma volume identical to the initial and a total red cell mass slightly but insignificantly lower, with no remarkable changes in indices. K-2, who showed a fall in plasma volume of 13.4 per cent, in blood volume of 17.6 per cent, and in total red cell mass of 24.6 per cent during the second week on a dose of 2.1 Gm., now, on 16.5 Gm. in the fourth week, showed lowered plasma volume, constant blood volume, and total red cell mass values recovering. M, whose first week readings were -14.8 per cent for hemoglobin, -19.8 per cent for erythrocyte count, -7.1 per cent for venous hematocrit, and -11.3 per cent for total red cell mass on a dose of 4.2 Gm., now in the fourth week on a dose of 16.8 Gm. showed -7.4 per cent for hemoglobin, -5.7 per cent for erythrocyte count, -4.1 per cent for hematocrit, -14.7 per cent for plasma volume, -14.7 per cent for blood volume, and -20.9 per cent for total red cell mass, again demonstrating a further fall in total red cell mass without corresponding changes in the indices. At this point M developed dizziness, weakness, and ashen pallor, and the drug was discontinued. One week after discontinuation, the values of the three indices were within normal limits, whereas plasma volume was still -15.1 per cent, blood volume -16.9 per cent, and total red cell mass -19.2 per cent. Five weeks after discontinuation, the total red cell mass had risen to -8.4 per cent, the body weight remaining unchanged from initial.

SUBSEQUENT WEEKS. N-2, who had taken 10.4 Gm. in 12 days and showed a total red cell mass fall of 26.4 per cent and symptoms of dizziness and weakness, became weaker and more dizzy in the fourth week, and collapsed on getting out of bed. The veins were collapsed, and no blood tests could therefore be done. The drug was discontinued, and one week after the discontinuation venipuncture could again be done. The values were then -7.4 per cent for hemoglobin, -22.2 per cent for hematocrit, -10.4 per cent for plasma volume, -24.8 per cent for blood volume, and -41.6 per cent for total red cell mass, as against -3.7, +4.3, -14.9, +1.7, -11.2, and -26.4 per cent respectively in the second week.

In the fifth week, one witnesses the phenomenon of N-1, on 69.6 Gm. or 2.4 Gm. daily, still maintaining blood values within normal limits and scoring a gain of 16 per cent in body weight. N-2, whose reaction to the drug resulted in collapse and seemed to be the extreme opposite of N-1, had his drug discontinued for 10 days, then resumed on 300 mg. daily for another 19 days, and still showed -7.4 per cent for hemoglobin, -6.8 per cent for erythrocyte, -22.2 per cent for hematocrit, -24.8 per cent for blood volume, and

-41.6 per cent for total red cell mass, but with the weight +8.5 per cent above initial and the plasma volume at -10.4. Even seven weeks after discontinuation, the values were still -21.8 per cent for hematocrit and -18.7 per cent for total red cell mass. The plasma volume at this time was expanded to 23.4 per cent, but it is difficult to determine whether this was still due to the effect of the drug.

In the sixth week, in patient P-2, whose total dosage of the drug had reached 6.9 Gm., the blood values were almost the same as in the first week, when he had taken only 1.8 Gm., but by the fifteenth week, the total red cell mass had fallen to -20.6 per cent and the hematocrit to -11.5 per cent. In the eighth week, K-2's total red cell mass, which was -24.6 per cent the second week and -13 per cent the fourth week, now sank to -24.1 per cent on dosages of respectively 2.1 Gm., 16.5 Gm., and 46.8 Gm. In the seventh week, H-3, whose first week total red cell mass was -13.5 per cent, falling to -17.1 per cent the second week, and rising to +14.5 per cent the third, had risen to -8.3 per cent with doses of 8.4 Gm., 16.8 Gm., 25.2 Gm., and 57.6 Gm. respectively. K-2 in the twelfth week had scored a gain in body weight of 13.2 per cent and a rise in total red cell mass from a low of -24.1 per cent in the eighth week to only -5.5 per cent. H-3, in the fourteenth week on a dose of 116.4 Gm., had a total red cell mass practically the same as at the zero day, but had an expanded plasma volume of 21.5 per cent over zero day. P-1, the only other fourteenth week patient, had now restored almost all his premedication values, even though at this time he had taken 107.71 Gm. of the ataraxic.

COMMENTS

It will be seen from the above account that there was apparently great individual difference in the response of the blood picture to the effect of large doses of chlorpromazine. The responses were of four types: (1) Patients in whom there was no substantial change; (2) those in whom there was profound change from which there is recovery; (3) those in whom the only change was that of an expansion of the plasma volume, a phenomenon that, when attended by a fall in the indices, could have been misinterpreted as anemia; (4) those in whom the fall in total red cell mass was accompanied by dizziness, pallor, and even orthostatic collapse and discontinuation of the drug. Whether the orthostatic collapse was due solely to the drop in the total red cell mass or to the additional factor of sluggishness of the vasomotor pressure reflexes is not clear.

The hemoglobin and erythrocyte values in this study were not reliable indices to the size of the total red cell mass. The venous hematocrit was a more faithful but still an unreliable indicator.

In view of the discrepancy between the hemoglobin, erythrocyte, and even hematocrit readings, on the one hand, and the total red cell mass measurement, on the other, in order to obtain an accurate knowledge of the effect of a drug on the number of erythrocytes, it will be necessary to resort to the measurement of total red cell mass.

The fall in the total red cell mass in exceptional cases may start in the first week, but it is most pronounced in the second week. In exceptional cases it may not be evident until the fifteenth week.

HEMATOLOGIC STUDIES AND CHLORPROMAZINE

There is no apparent relationship between the length of hospital residence and the drug effects under study.

SUMMARY AND CONCLUSIONS

In a serial study of the blood volume and its formed elements in 7 psychotic patients, it was found that, if the body weight did not vary within ± 2 per cent, the hemoglobin value varies from week to week between -10 and +11 per cent, the erythrocyte count between -20.7 and +25.8 per cent, the venous hematocrit between -6.5 and +8.6 per cent, the plasma volume between -8.9 and +3.25 per cent, the blood volume between -5.3 and +10.1 per cent, and the total red cell mass between -14.3 and +10.1 per cent.

In a similar study of 15 patients under chlorpromazine, it was found that the hematologic response of patients to the effects of chlorpromazine was subject to great individual variation, and that patients with four types of response were encountered: (1) Those whose blood values were unaffected even with large doses; (2) those whose only change was in an expansion of the plasma volume; (3) those in whom there was a marked fall in the total red cell mass followed by recovery of the lost values; (4) those in whom the fall in total red cell mass was not followed by a recovery and in whom marked dizziness, weakness, and even orthostatic collapse necessitated discontinuation of the drug.

The hemoglobin level, the erythrocyte count, and the venous hematocrit were not reliable indices to the total red cell mass.

ACKNOWLEDGMENT

Thanks are due to Smith, Kline & French for the generous supply of chlorpromazine used in the study.

RESUMEN

En un estudio seriado de la sangre y de sus elementos figurados, de la sangre de 7 psicóticos, se halló que, si el peso corporal no variaba dentro del ± 2 por ciento, la hemoglobina variaba de una semana a otra entre -10 y +11 por ciento; los eritrocitos entre -20,7 y +25,8 por ciento; el hematocrito, entre -6,5 y +8,6 por ciento; el volumen del plasma entre -8,9 y +3,25 por ciento; el volumen sanguíneo entre -5,3 y +10,1 por ciento, y la masa total de glóbulos rojos entre -14,3 y +10,1 por ciento. En un estudio similar de 15 pacientes tratados con clorpromazina, se halló que la respuesta hematológica estuvo sujeta a grandes variaciones individuales. En este sentido, se hallaron cuatro tipos de respuesta: (1) pacientes cuyos valores hemáticos no fueron afectados ni siquiera con grandes dosis; (2) enfermos en los cuales hubo solamente un aumento del volumen plasmático; (3) pacientes en los cuales se produjo un descenso notable de la masa total de glóbulos rojos, seguido de la recuperación de los valores bajos; (4) pacientes en los cuales el descenso de la masa de glóbulos rojos no fue seguido por una recuperación y en los cuales un intenso mareo y debilidad, e incluso colapso ortostático, hizo necesario suspender la administración de la droga. La concentración de hemoglobina, el conteo eritrocítico y el hematocrito no fueron índices apropiados para evaluar la masa total de glóbulos rojos.

RESUME

Dans une étude en série du volume du sang et de ses éléments figurés chez 7 psychotiques, il a été observé que si le poids du corps ne varie que dans les limites de 2 % en plus ou en moins, la valeur de l'hémoglobine varie de semaine en semaine entre -10 % et +11 %, le nombre des hématies entre +20,7 % et +25,8 %, l'hématocrite veineux entre -6,5 % et +8,6 %, le volume plasmatique entre -8,9 % et +3,25 %, le volume du sang entre -5,3 % et +10,1 %, la masse totale des hématies entre -14,3 % et +10,1 %. Une étude similaire comprenant 15 malades soumis à la chlorpromazine a révélé que la réponse hématoologique des malades aux effets de la chlorpromazine était sujette à de grandes variations individuelles; chez ces malades il a été observé quatre types de réactions: 1) cas où les valeurs hématologiques n'étaient pas modifiées, même par des doses fortes; 2) cas où la seule modification observée était l'accroissement du volume plasmatique; 3) cas où une chute prononcée de la masse totale des hématies était suivie de la reprise de la valeur perdue; 4) cas où la chute de la masse totale des hématies n'étaient pas suivie de récupération, et dans lesquels les vertiges marqués, l'asthénie, parfois même le collapsus orthostatique a nécessité l'interruption de la drogue. Le taux de l'hémoglobine, le nombre des hématies et l'hématocrite veineux ne constituaient pas des indices sûrs quant à la masse totale des hématies.

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Annual Meeting of Academy of Psychosomatic Medicine

The sixth annual meeting of The Academy of Psychosomatic Medicine will be held October 15 through 17, 1959, at the Sheraton-Cleveland Hotel in Cleveland. The meeting will be oriented to the needs of nonpsychiatric physicians. Practical everyday office management of psychosomatic problems and emotional disturbances will be dealt with in formal papers, symposia, panel discussions, and small study groups. The meeting will be open to all scientific personnel, including psychologists, social workers, and nurses. Information may be obtained from Dr. Bertram B. Moss, Suite 1035, 55 East Washington Street, Chicago 2, Ill.

Psychological Response to *d*-Lysergic Acid Diethylamide and Its Relationship to Adrenochrome Levels

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SASKATOON, SASKATCHEWAN

d-Lysergic acid diethylamide-25 (LSD) causes psychological changes in normal people that closely resemble the experiences described by some sufferers from schizophrenia. Those authorities who deny this have based their objection on a comparison of the first or second experience of volunteers for LSD with well-established schizophrenia where the symptoms have been present for months and years. It seems more logical to compare either the first LSD experience with the early stages of schizophrenia of rapid onset or the LSD experience of volunteers who have used it several times with schizophrenia of longer duration. When this is done the analogy is much closer.

Although it is rarely emphasized, the psychological study of this hallucinogen, as with that of mescaline, has far outdistanced our understanding of the meaning of the biochemical and physiological responses to taking it. These biochemical and physiological responses have still to be related to the psychological changes in some comprehensible manner. At least three biochemical hypotheses based upon some known *in vitro* and *in vivo* properties of LSD can be developed. First, because LSD is a potent antiserotonin, using uterine muscle as an indicator, it has been suggested that there is an analogous activity in the brain, which is known to contain serotonin. However, since other LSD isomers and brom-LSD, which are not hallucinogenic, are more strongly antiserotonin in the same test system, this suggestion seems implausible. Second, LSD, a potent acetylcholine esterase inhibitor, elevates brain acetylcholine levels. Other substances that are esterase poisons, such as diisopropyl fluorophosphonate and others, also produce remarkable psychological changes. Yet this in itself can not be a main factor because brom-LSD, which is not a hallucinogen, is equally strong as an esterase poison. Third, there may be some interference in the intermediary metabolism of the sympathomimetic amines, noradrenaline and adrenaline. A substantial quantity of data suggests that this may be the key factor. Of course, biochemical changes are not as a rule isolated from other changes. One disturbance in metabolism produces changes in all the allied areas. It is likely LSD has its unique action

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because it interferes in adrenaline utilization, poisons choline esterase, and is an anti-metabolite of serotonin. Similar compounds, such as *d*-iso-LSD, might share two but fail in one of these attributes and would therefore not be hallucinogenic.

The psychological change in people who are mentally ill or who are given LSD is apparently more clearly associated with adrenaline metabolism than with the parasympathetic, which in turn is more heavily involved than serotonin. Anxiety, which is a function of adrenaline secretion, may become very intense, remain moderate, or disappear within the first hour after taking an adequate quantity of LSD. During this period, plasma adrenaline levels show substantial fluctuations. Physiologically, autonomic changes are marked. A very constant finding is pupillary dilatation. This in itself is a useful index of LSD activity. One of the major sites for the production of adrenaline, the adrenal medulla, shows an increase in metabolic activity, i.e., the radio phosphorus uptake is markedly increased. This is specific for the medulla since there is no comparable change in the cortex.

Adrenochrome and adrenolutin are readily formed from adrenaline *in vitro*¹⁰ using either plasma or enzymes extracted from biological tissue. It would be surprising if similar activity did not occur *in vivo*. In fact, these substances have been extracted from human and animal tissues. Furthermore, it has long been suggested that there is a relationship between adrenaline and pigmentation. Pigment formation must be through some preliminary indole reaction followed by polymerization. Finally, they produce psychological changes in man and behavioral change in animals. The evidence is reviewed by Hoffer and Osmond,⁹ where references for these statements are given.

Adrenolutin in normal volunteers produced changes in phosphate excretion similar to those induced by LSD.

We have examined further the possible relationship of LSD to adrenaline metabolism by: (1) measuring the effect of LSD on adrenaline oxidase,¹⁰ (2) measuring the effect of LSD on *in vitro* conversion of adrenaline to adrenolutin, (3) measuring the *in vivo* plasma adrenochrome levels after administration of LSD, brom-LSD, and lysergic acid morpholide (LSM).

METHOD

The activity of adrenaline oxidase was determined by measuring the conversion of adrenaline into adrenolutin.⁴ Adrenochrome was measured by converting adrenochrome in the plasma to adrenolutin and determining the fluorescence in the Farrand spectrophotometer (excitation at 405 μ , emission maximum at 500 μ).⁹ The ascorbic acid factor was measured in the manner described by Hoffer.⁵ This factor is a measure of the bleaching of plasma by ascorbic acid after incubation with adrenaline. Adrenochrome was synthesized by Heacock et al.³

Our subjects were healthy normal volunteers, who received payment, and physically healthy alcoholics (character disorder and psychopathy), who received these compounds for therapy.^{1, 11}

Blood was drawn in the morning, while fasting, into heparinized flasks. The subjects were then given 100 to 300 μ g. of LSD, and blood samples were taken at intervals during

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TABLE I
Effect of d-LSD-25 and of Various Diagnostic Groups on Conversion of Adrenaline into Adrenolutin and into AAF

Group	Number	Adrenolutin O.D.* at 395		Ascorbic acid factor bleaching at 420	
		Mean	Range	Mean	Range
Alcoholics, LSD					
0 time	5	0.36	(0.24-0.62)	0.17	(0.01-0.41)
2 hours	5	0.48	(0.21-0.94)	0.27	(0.05-0.54)
5 hours	5	0.40	(0.39-0.62)	0.24	(0.10-0.53)
7 hours	5	0.36	(0.25-0.49)	0.24	(0.12-0.34)
Normal	18	0.30	(0.17-0.45)	0.10	(0.01-0.29)
Nonschizophrenic	15	0.31	(0.15-0.42)	0.07	(0.02-0.24)
Schizophrenic					
Before treatment	13	0.35	(0.08-0.54)	0.21	(0.05-0.36)
After treatment	11	0.35	(0.17-0.49)	0.06	(0.02-0.11)
Surgical					
Before operation	28	0.36	(0.24-0.69)	0.13	(0.03-0.35)
During operation	12	0.43	(0.26-0.61)	0.22	(0.02-0.50)

* Optical density measured in spectrophotometer.⁴

and after the experience. In some instances, normal volunteers were treated before and/or during the experience with large quantities of ascorbic acid. During the whole experience every subject was carefully observed by a trained psychiatrist.

RESULTS

Effect of LSD upon Adrenaline Oxidase. The effect of LSD upon adrenaline oxidase activity (conversion of adrenaline into adrenolutin) is shown in table I. LSD increased the ability of plasma to convert adrenaline to adrenolutin. The ascorbic acid bleaching factor was also increased from 0.17 to 0.27 at two hours. The same table shows adrenaline conversion values and ascorbic acid factor for volunteers, psychiatric patients, and non-psychiatric patients before and during surgical operation. Schizophrenic and surgical patients before operation had a little more adrenaline oxidase than normal and nonschizophrenic controls. The highest concentration was found when blood was drawn during operation. These high values are probably due to slight hemolysis of the erythrocytes due to surgical trauma. Small quantities of freshly liberated hemoglobin catalyzes the conversion of adrenaline to adrenolutin.^{5, 10}

Patients about to undergo surgery are usually apprehensive. This might account for the increases in their adrenaline oxidase. These values were comparable to the initial values in the 5 alcoholics before receiving LSD. The two hour LSD values are higher than those found in patients undergoing surgery. This cannot be entirely due to stress, for many patients who have been given LSD are quite relaxed and at ease two hours after

it has been administered. It is probably due to a direct effect of LSD on adrenaline oxidase concentrations in blood.

There is a good relationship between the ascorbic acid factor (AAF), diagnosis, stress,

TABLE II
Effect of d-LSD-25 on Adrenochrome and on Experience

Subject	Adrenochrome			Experience				
	Init.	Max.	Change, %	Anxiety	Perception	Paranoid	Affect	Withdrawal
	μg./liter							
Mrs. Y.A.								
First	92	84	-9	Intense	Slight	-	-	-
Second*	84	135	+61	Slight	Moderate	-	-	-
Third	78	171	+119	Moderate	Moderate	+	-	-
Mr. M.A.	194	190	-2	Intense	Slight	-	-	+
Mr. K.A.	62	131	+111	Moderate	Moderate	+	-	+
Miss J.E.	22	71	+223	Moderate	Moderate	+	-	+
Miss D.O.								
First	61	30	-50	Intense	Slight	-	-	+
Second*	44	122	+177	Slight	Moderate	-	-	-
Mr. R.O.	45	81	+80	Moderate	Moderate	+	-	+
Mr. N.O.								
First	48	91	+89	Intense	Slight	-	-	-
Second*	47	125	+163	Moderate	Moderate	-	-	-
Miss H.A.	62	212	+242	Moderate	Moderate	+	+	+
Miss N.E.	66	106	+61	Moderate	Slight	-	-	-
Miss W.I.	88	166	+89	Intense	Intense	+	+	-
Mr. C.H.	54	346	+540	Slight	Slight	-	+	-
Mr. D.I.	76	185	+143	Moderate	Intense	-	-	-
Mr. R.Y.								
First	54	166	+208	Moderate	Moderate	-	-	-
Second	61	239	+292	Slight	Slight	-	-	-
<i>Ascorbic acid given during or before experience</i>								
Miss D.A.	78	105	+35	Intense	Moderate	-	+	+
Miss H.O.	83	72	-13	Slight	Intense	-	+	-
Miss E.L.	64	83	+30	Slight	Moderate	-	+	-
Miss G.A.	51	87	+70	Slight	Moderate	-	+	-
Miss O.L.†	90	236	+162	Slight	Intense	-	-	-
<i>Adrenochrome levels in urine</i>								
Mr. B.L.	152	231	+52	Slight	Intense	-	+	+
Mr. B.O.	220	500	+127	Slight	Moderate	-	-	-

* 10 mg. of adrenochrome given intravenously.

† Ascorbic acid only before LSD.

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and LSD. Normal subjects, nonschizophrenic psychiatric patients, and schizophrenics who had been improved by treatment had the lowest quantity of AAF. Schizophrenic patients, before treatment, had AAF values comparable to patients undergoing surgery and alcoholics before receiving LSD. The highest AAF values were reached two hours after receiving LSD and then remained high up to seven hours. AAF is probably a combination of some adrenaline derivative and some plasma constituent, perhaps with hemoglobin. AAF can be increased by hemoglobin, adrenochrome, adrenolutin, or by incubating plasma with adrenaline. It is a factor that is bleached by ascorbic acid, as is adrenochrome or hemoglobin.

The Effect of LSD, 2-Bromolysergic Acid Diethylamide and LSM on Psychological State and Adrenochrome Levels. LSD produced the usual reactions in our subjects. Most alcoholics responded less and so required larger quantities to induce well-marked reactions.^{1, 11} 2-Bromolysergic acid diethylamide (BOL) did not produce any LSD-like experiences (500 µg. in normals) but did produce mild increases in tension. LSM (150 µg.) did not produce any psychological changes resembling those induced by LSD. Mild anxiety similar to what we have obtained with placebo was produced. The effect of LSD upon adrenochrome plasma levels is shown in table II. Neither BOL or LSM increased adrenochrome.

TABLE III
Relationship of Increase in Plasma Adrenochrome to Aspects of the Psychological Experience

Category of change	Number	Adrenochrome levels, µg./liter		
		Initial	Maximum	Increase, %
Perceptual				
No or slight change	7	82	154	88
Moderate change	9	54	125	100
Intense change	2	82	176	114
Anxiety				
None or slight	4	61	211	246
Moderate	9	57	127	123
Intense	5	97	112	15
Paranoid symptoms				
Absent	12	72	152	111
Present	6	60	139	132
Affective change				
Absent	15	69	128	88
Present	3	68	241	254
Withdrawal				
Absent	12	66	161	144
Present	6	74	119	60

The Effect of Ascorbic Acid Given in Large Quantities Before and During LSD. Ascorbic acid decreased the intensity of the experience slightly but altered its quality. Among unsophisticated subjects LSD usually produced moderate or marked perceptual change, disturbance in thought, and marked fluctuation in mood from elation to depression, more frequently depression. With ascorbic acid, perceptual changes were not altered. Disturbances in thought were less marked, and suspicion was less evident. The ability to concentrate and appreciate the perceptual changes was heightened. Mood swings still occurred, but the subjects tended to be cheerful and/or euphoric. Four subjects took the combination and LSD alone, and they have confirmed these conclusions.

In table III subjects are grouped according to the psychological response. Perceptual changes and paranoid symptoms did not depend upon the level of adrenochrome. When the level of adrenochrome was high, much less anxiety was seen. Affective changes were marked and withdrawal less frequent with greater adrenochrome response.

When ascorbic acid was given during the LSD reaction, the level of plasma adrenochrome did not increase except for 1 subject (O.L.) who received ascorbic acid several days before and not during the experience.

Effect of LSD, d-Lysergic Acid Ethylamide, and BOL upon Conversion of Adrenaline to Adrenolutin. Although LSD and d-lysergic acid ethylamide (LAE) increased the in vitro conversion of adrenaline to adrenolutin, BOL had no effect. (See table IV.)

Effect of LSD and BOL on Adrenochrome Tolerance Curves. Crystalline adrenochrome dissolved in water or saline solution is quickly destroyed when injected intravenously. The rate of destruction was measured by estimating the plasma adrenochrome values, 15, 30, and 60 minutes after injecting 10 mg. The amount of plasma adrenochrome for different psychiatric conditions and after pretreatment with LSD is shown in table V.

TABLE IV
Effect of LSD, LAE, and BOL upon Conversion of Adrenaline to Adrenolutin in Vitro

Subject	Control	Formation of adrenolutin as measured by increase in optical density at 395 μ		
		d-LSD-25, 50 gamma	LAE, 50 gamma	BOL, 50 gamma
1	0.250	+64	+32	—
2	0.210	+37	+62	—
3	0.240	+12	+42	—
4	0.352	+12	+26	—
5	0.256	+10	+22	—
6	0.410	—	—	-11
7	0.332	—	—	0
Mean	0.260	+27	+37	-6

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TABLE V
Relationship of Adrenochrome Tolerance to LSD and BOL

Group	Treatment	Number	Initial adrenochrome	% change		
				15 min.	30 min.	60 min.
Not schizophrenic	None	9	51	+170	-45	-22
Schizophrenic	None	6	43	+280	+75	+107
Not schizophrenic	LSD (35 µg.)	6	43	+260	+100	+67
Not schizophrenic	LSD (100 µg.)	2	46	—	—	+170

In nonschizophrenic subjects all the injected adrenochrome was destroyed within 30 minutes. However, in schizophrenics, 60 minutes after injection the plasma levels were twice the base line level.

Normal volunteers in whom all the adrenochrome was destroyed in 30 minutes in a previous experiment were given 35 µg. of LSD by mouth and the adrenochrome injected two hours later. One hour after the injection some of the adrenochrome was still circulating. It would appear that the reduced ability of schizophrenics to destroy adrenochrome is equal to the effect of 35 µg. of LSD. Perhaps we can use this adrenochrome tolerance test to develop a titer for schizophrenia. After 100 µg. of LSD, the ability to destroy adrenochrome was markedly reduced. BOL did not alter the adrenochrome tolerance.

DISCUSSION

We define a good LSD experience as one in which insight is maintained and during which the subject feels he has been drawn closer to humanity and away from autism. This may be associated with vivid perceptual changes, especially during the first or second experience, but may occur in the absence of visual changes.

We have found that "good" experiences seem to be associated with substantial increases in plasma adrenochrome levels. The subjects were less anxious and were aware of fluctuations of mood from depression to euphoria with little tendency to withdraw from other people in the experimental setting. When plasma adrenochrome levels did not increase, the subjects remained very anxious and tense. In some instances the tension was of psychotic proportions. They complained primarily of depression and found it difficult to participate with other subjects. Paranoid thinking and visual changes occurred independently of adrenochrome levels.

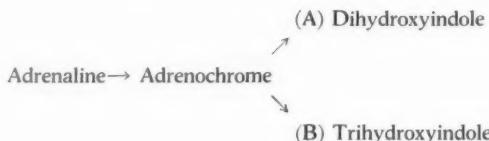
Alcoholics treated with LSD do better clinically after an intense experience (little anxiety).^{6, 11} Alcoholics and other subjects subject to great tension or subjects especially tense before receiving LSD tend to become more tense or depressed and usually do not benefit from the experience. Giving them more LSD does not necessarily produce a better reaction but may increase the tension. Much of the tension may be removed by the intravenous injection of adrenochrome or adrenolutin. This allows the more desirable aspects of the reaction to appear. Subject Y.A. was very anxious the first time she received LSD.

Two hours after getting LSD the second time, she was given 10 mg. of adrenochrome. The third time she received LSD, several weeks later, she was relatively free of anxiety. Subjects D.O. and N.O. also received 10 mg. of adrenochrome two hours after LSD. In each case intense anxiety with slight perceptual change was replaced by slight or moderate anxiety and an increase in perceptual change.

Since the plasma adrenochrome value is clearly related to the psychological experience after LSD, it seems likely that it is the intermediate by which LSD acts. BOL, which like LSD antagonizes serotonin and poisons choline esterase, has no effect on adrenochrome levels.

Adrenochrome is converted in vitro by many reducing substances into at least two classes of compounds: (1) dihydroxyindoles and (2) trihydroxyindoles.² The major dihydroxyindole is 5,6-dihydroxy-N-methylindole. Melander⁷ found that adrenochrome reduced by ascorbic acid is not psychotomimetic for animals. We have found in a large series of tests with volunteers that this pure indole is not psychotomimetic. Adrenolutin is the best-known example of the trihydroxyindoles. It is a pale yellow highly fluorescent psychotomimetic substance. In vivo, adrenochrome may thus be converted into either the dihydroxy or trihydroxy series depending upon the biochemical conditions.

These changes can be shown diagrammatically thus:



We suggest that reaction A is the preferred pathway, and that LSD poisons the enzyme that catalyzes this reaction. As a result there is: (1) An increase in adrenochrome since it is not destroyed so quickly and the excess appears in blood and urine, (2) some diversion of the adrenochrome into adrenolutin, and (3) consequently a decrease in the rate of destruction of injected adrenochrome. This inhibition probably occurs in the brain as well as peripherally.

The psychological experience produced by LSD continues long after practically all the compound has been either destroyed or excreted. If the suggestion that the enzyme necessary to reaction A is poisoned is correct, then it would account for the prolonged psychological reaction. Many natural enzymes are regenerated rather slowly.

Ascorbic acid converts adrenochrome into both types of compounds. It therefore prevents any increase in concentration of adrenochrome without interfering with the production of adrenolutin and the other indoles. This may be why large quantities of ascorbic acid do not inhibit but merely alter the nature of the LSD experience. It is also possible that ascorbic acid has less effect upon intracellular adrenochrome in the brain and elsewhere than upon extracellular adrenochrome.

Ascorbic acid altered the experience by decreasing depression, withdrawal, and paranoid

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thinking. Perhaps these psychological reactions are a function of adrenochrome concentration rather than of adrenolutin.

SUMMARY AND CONCLUSIONS

d-Lysergic acid diethylamide-25 elevates plasma adrenochrome, reduces the ability of the blood to destroy adrenochrome, and increases the conversion *in vitro* of adrenaline into adrenochrome and adrenolutin by plasma. 2-Bromolysergic acid diethylamide has no effect on adrenochrome. We therefore suggest that *d*-lysergic acid diethylamide-25 inhibits an enzyme responsible for the conversion of adrenochrome into dihydroxyindoles.

ACKNOWLEDGMENT

The *d*-lysergic acid diethylamide-25 used in this study was provided by Sandoz and Company of Canada. The scientific interest of this company and their medical director, Dr. Grosheintz, has been most helpful to our research program.

RESUMEN

El compuesto ácido *d*-lisérgico-diatilamida-25 eleva el adenocromo del plasma, reduce la capacidad de la sangre para desintegrar el adenocromo y aumenta la proporción de conversión del plasma, *in vitro*, de la adrenalina en adenocromo y adrenolutina. El ácido 2-bromolisérgico-dietilamida no ejerce acción alguna sobre el adenocromo. Por esto, sugerimos que el ácido *d*-lisérgico-dietilamida-25 inhibe una enzima responsable de la conversión del adenocromo en dihidroxiindoles.

RESUME

L'acide *d*-lysergique-diéthylamide-25 élève l'adrénochrome du plasma, réduit la capacité du sang à détruire l'adrénochrome et à augmenter *in vitro* la conversion de l'adrénaline en adrénochrome et en adrenolutine par le plasma. Le diéthylamide de l'acide 2-bromolysérgique est dépourvu d'action sur l'adrénochrome. En conséquence, nous présumons que l'acide *d*-lysergique diéthylamide-25 inhibe un enzyme responsable de la conversion de l'adrénochrome en dihydroxyindoles.

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Annual Workshop in Projective Drawings

The 1959 Annual Workshop in Projective Drawings, to include the House-Tree-Person, Draw-A-Person, Draw-A-Family, Unpleasant Concept, Draw-An-Animal, and Eight Card Re-Drawing tests, and doodles, will be conducted at the New York State Psychiatric Institute, New York City, by Emanuel F. Hammer, Ph.D., and Selma Landisberg, M.A., July 27 through July 30, 1959, from 9:30 a.m. to 12 noon and from 1:30 p.m. to 3 p.m. daily. The workshop will provide a grounding in fundamentals, advanced considerations of differential diagnosis, psychodynamic appraisal, psychological resources as treatment potentials, and the application of drawings in therapy. Requests for information on admission or requirements should be addressed to Miss Selma Landisberg, 116 East 35th Street, New York 16, N. Y.

Karen Horney Award

The Association for the Advancement of Psychoanalysis announces the establishment of the Karen Horney Award. The purposes of the award are twofold: The first is to commemorate Karen Horney, who, pioneering in the integration of various scientific disciplines, deepened our understanding of human motivation, and who was a founder of the American Institute for Psychoanalysis and of the Association for the Advancement of Psychoanalysis. The second is to stimulate research in the theory and practice of psychoanalysis and to underline the new developments in psychoanalysis and related sciences. The award will be in the amount of \$150 and will be made to the author whose paper makes such a contribution to the advancement of psychoanalysis. The paper will be published in the *American Journal of Psychoanalysis*, the journal of the association, and should be submitted by October 31, 1959. The award will be presented at the time of the Karen Horney Memorial Lecture, which usually is given in March. Entries should be forwarded to Louis E. DeRosis, M.D., Chairman, Award Committee, 815 Park Avenue, New York 21, N. Y.

A Nascent Somatic Delusion Treated Psychotherapeutically by a Confrontation Technique

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Early in Freud's writing he distinguished between obsessions and phobias.¹ The components of an obsession he described as an idea that forces itself on the patient against his conscious wish, and an associated emotional state in which doubt, remorse, or anger may occur. The obsession is distinguished from the phobia in that fear is the dominant mental state of the latter. The emotional state is persistent, and the obsessive idea is substitutive of an original one. The original idea is to be found in the past life experience of the patient. The replacing idea symbolizes a more acceptable, even if maladaptive, substitute for some very painful experience in the patient's libidinal life that he is trying to forget. Inappropriate or ceremonial acts can be similarly substitutive. They were also described as obsessive acts and compared to religious rituals. The experiencing of anxiety and pangs of conscience on their omission, and their relative complete independence from all other conventional activities, were noted as characteristic. A general sense of guilt that is hard to rationalize dominates the sufferer. It has its origin in certain earlier psychological events, but is constantly revived by current "temptation." It gives rise to a state of anxious expectation or anticipation of misfortune, which through the idea of punishment is linked with the inner perception of temptation to indulge in a forbidden impulse, and its subsequent repression. A certain amount of energy is consciously directed against the completion of the impulse, but the process of repression may not be successful. Ceremonial and obsessive acts then arise as a further defense against yielding to such temptation. These protective measures may also begin to fail. Further prohibitions then come into play in order to keep at a distance the self-forbidden desires or ideas.

Most frequently encountered in medical practice is the idea that a certain symptomatic sensation symbolizes a popularly conceived malignant or fatal disease, such as cancer, polio, or heart disease. In earlier generations, a belief in the prevalence of the venereal diseases served this same type of phobic purpose. The curability of the diseases and changes in our mores about sexual feelings and behavior have eliminated the phobic function of concern about venereal infection. One does not encounter the emotional state of "doubt, remorse, or anger" in the phobic picture. Fear is the dominant emotion.

A different type of obsessive idea may be the relatively fixed somatic delusion. A false conviction is generated that there has actually taken place a change in body appearance. Or there may be generated the conviction that surgical procedures, usually on the nose, face, or bosom, will solve social and psychological problems. There may be no significant disorganization of thinking, nor may there be any admixture of hypochondriacal sympto-

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matology of a more diffuse nature. This phenomenon has also been referred to as an "idée fixe." Marked preoccupation with this alleged or proposed body change, or with some imperceptible "defect," is the predominant symptom. Massive neurotic or psychotic syndromes are generally associated with such fantasies of body change or grossly exaggerated concerns about alleged blemishes. However, the patient with an obsessive neurotic disturbance may easily be distinguished from the psychotic patient by his ability to perceive that his preoccupation with a body change, a disease, or an act is quite different from effecting the body change, having the actual disease, or performing the act. Delusional thinking may be described as occurring when (1) there is a belief that something is a true fact that actually is not so; (2) this error in perception cannot be corrected by an "appeal to reason" of the person entertaining it; and (3) adherence to the false perception is out of harmony with what may reasonably be expected in the light of the individual's education, social status, and customary mode of thinking and reacting.

The patient with a fixed somatic delusion but who has good mental organization and is relatively free from other hypochondriacal ideas is rarely seen, in contrast to the more frequent appearance of patients with somatic delusions in the more advanced or deteriorated psychotic states. It has been the experience of most therapists that the treatment of a patient with a fixed somatic delusion is usually a very frustrating problem. Seldom is such a patient seen by a psychiatrist until he has had a series of examinations and unsuccessful treatments by biochemical and sometimes even by surgical procedures. By this time, the condition has become quite fixed and its antecedent experiences and associations are buried deeply under an overlay of manipulation and repression.

The surgeon is faced with distressing frequency by the necessity of dealing with an urgent request for some alteration of the body form. The patient, in a self-deluded fashion, anticipates from this alteration a change in personality, the achievement of certain aspirations, and a generally improved success in living. Unfortunately, the folklore of our society, supported by advertising and the mass communication media, tends to support such a mistaken assumption on the relationship of outer form and success in living. Clothes are presumed to make the man. Popular psychology glibly interprets Napoleon's drive to greatness as a reaction formation to small stature. Short men who fail or experience anxiety in love and work want to succumb to the suggestion that elevated shoes, rather than some inner change, will pave the way to success and happiness. The development of plastic surgery has similarly raised the widespread but deluded hope that an alteration in the shape of a nose, the removal of a facial blemish, or the surgical modification of a bosom will, without further effort, bring success in love, work, and interpersonal effectiveness generally. The doctor no less than the patient is sometimes culture bound in the sense that he may be influenced by the folklore of the social groups of which he and the patient are both members. Barker² and others have pointed out a constant bias in our society to overestimate the potential psychological malignancy of a physical disability, as well as to overestimate the power to effect improvement in a person's total life by improvements in mechanical physiology alone. The physical rehabilitation, to become functional, needs an associated psychosocial alteration, often involving a total readjustment of the person.

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What needs to be determined, in dealing with the isolated somatic delusion, is the unsolved psychological problem or conflict for which this symptom provides a temporary but pathological solution. Similarly, in the decision to alter the body form surgically, an investigation of the motivation, sources of anxiety, and nature of the problem to be "solved" by this act is in order. MacGregor³ and Hill and Silver⁴ have convincingly shown the urgency of understanding psychosocial factors in evaluating the request and in reaching a responsible medical decision on whether and how the request for surgery should be granted.

In a study of a continuous series of patients requesting plastic surgery, with no other complaints, the overwhelming number of latent neurotic problems thus elicited led to the conclusion that it would not be much of an exaggeration to state categorically that the desire leading to actual consultation of the surgeon should be regarded as a symptom of neurosis. Too often, without concurrent planning and treatment on the physiological, psychological, and sociocultural level, a sudden alteration of body form may constitute so abrupt a removal of a defensive system and present so many more unsolvable problems of readjustment as to generate overwhelming anxiety, precipitate a neurosis or a psychosis, and even lead to paranoid litigious attacks on the physician. Too often is the patient referred to psychiatry after surgical intervention has decompensated the neurosis of an allegedly "normal" person, who, in the mind of the surgeon, simply required some cosmetic improvement the better to meet certain desirable social standards. Occasionally the psychiatrist also receives the patient who has not been helped by surgical intervention for a somatic delusion. One such patient was recently seen diagnostically by the author and complained of a distortion of his forehead. "Can't you see how large these lumps are?" Aside from this one delusional idea, there was no other manifest evidence of delusional thinking, disorganization of any mental process, or such other ascertainable symptomatology to warrant considering him psychotic. He might have fitted some atypical diagnostic label such as "pseudoneurotic schizophrenia." This patient, prior to being seen by the author, had been successively treated by physician after physician in general practice, and by "psychotherapy" of an authoritative directive nature. He then proceeded to hypnosis and psychoanalytically oriented psychotherapy, which was also unsuccessful in removing the symptom, and which even failed to elicit the problem or conflict underlying the delusion. Finally, shock therapy and lobotomy were tried with no greater success. The patient's total interest centered on the urgent necessity of curing him of the lumps, and many physicians yielded to his urging to help him in differing ways. To fantasy about the symbolic meaning of the symptom can do little good.

The treatment of choice would seem to have been psychoanalytically oriented psychotherapy. It may well be that the succession of treatments before this type of therapy was finally attempted made the underlying conflict inaccessible. Ample reassurance and acceptance of the symptom as a private matter that need not be a source of concern or communicated to others in the absence of other problems would have spared patient and doctors much wasted time and resources until the treatment of choice could be satisfactorily initiated. Unfortunately, this patient's course is all too commonly the treatment experience of one with such a complaint, just as acceptance of the patient's request for

surgical intervention to "improve" the body form is too often accepted at face value, sometimes to the bizarre length of altering the sexual role.

Recently, the author had the unusual experience of treating a patient with a fixed somatic delusion immediately at onset, with the symptom in a nascent state. She had been seen by only one physician, her obstetrician, who immediately referred her for psychotherapy. It is only intended in this report to describe enough of the features of the case to show the nascent stage of a somatic delusion so that the dynamics of the psychopathology relating to this one symptom can be readily understood. A special treatment technique that has been developed by the author since 1951 made the psychodynamic factors appear in bold relief within the first interviews. It brought about the resolution of the acute presenting symptom and an awareness on the part of the patient of the need for a more thoroughgoing investigation and course of help for her difficulties.

The treatment technique requires some further elaboration. It can best be described as a special activity in psychotherapy that may be designated as "confrontation technique." A statement, command, or verbal expression is followed by the request, "What do you think of what I told you?" This technique involves the interjection of the confrontation into a psychoanalytically oriented psychotherapeutic process in which free association is the basic rule, and in which the interpretation of resistance is the outstanding activity of the therapist. From time to time the patient may be asked what his thoughts are, or what he "thinks now" about what was used as the "confrontation statement." Such interventions may be made when material directly related to the statement is being expressed, or when the material is such as to be considered derivative or substitutive of a reaction to the statement. The nature of the command or statement varies with the goals of therapy, the personality structure of the patient, or the nature of the currently most disturbing conflict. Usually it is a conflict situation about which the patient is conscious, or which seems to be operating in the preconscious.

The statements may be classified as: (1) A prohibition, or super ego statement: "I don't want you to masturbate under any circumstances." (2) An id or activity statement: "I want you to masturbate whenever you feel the urge." (3) An ego statement involving mature value orientations: "Masturbate at times and under circumstances when you can enjoy it without offending others or getting into trouble." It must be stressed that a statement is never made without a subsequent query: "What do you think about what I told you?" It varies from the parameters of psychoanalytic therapy as described by Eissler⁵ in that the patient is directly invited to tell what he thinks about what was told him. In psychoanalytic therapy the invitation to tell what the patient thinks about is inherent in the basic rule. Techniques utilizing the creation of psychological stress are coming into more general usage. Recently Cameron⁶ and Grinker and his group⁷ reported experiments in which stress statements were presented for the purpose of studying characteristic reactions to induced anxiety. Wolpe⁸ uses conditioning statements similarly.

Patient responses to the presented statement are almost uniformly characteristic, obvious, and predictable reactions, depending upon many factors that need to be studied. These include the individual patient, his transference attitudes and feelings at the moment, and

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the immediate setting in which the statement is made. Feelings of intense anxiety and fear may come into conflict with compliance and a desire to please. Anger, indifference, surprise, and other expressive reactions may be immediately noticed.

The nascent somatic delusion involved the presence of such disfiguring circles around the eyes as to confine the patient to her home, with an associated depressive affect. The husband of this 31 year old housewife kept the first appointment for his wife, who declined to come after the visit had been arranged by her obstetrician. He reported that his wife had been depressed since the death of their child shortly after delivery. "She is afraid to see people, wondering what they will think." Delivery had taken place about one month prior to the visit. She became preoccupied with ruminating over "what she could have done to bring about this misfortune," stopped doing her housework, refused to leave her home to shop or to see anyone socially, and remained in bed as long as she possibly could. He felt that there had been something unusual in her failure to purchase anything for the expected child beforehand. He was also impressed with the fact that during their first six years of marriage the sexual act had not been consummated with sufficient penetration to rupture the hymen. She conceived shortly after dilatation, which was advised by a gynecologist, through the use of "glass tubes." But she accepted this advice only after recovering from mumps, an illness that she believed might have affected her reproductive organs or rendered her infertile. She then became more relaxed and accepting of sexual relations. Prior to the above events, entrance was avoided by the husband because of her complaints of pain upon his attempting intercourse.

The patient kept the second appointment, which her husband arranged. Her appearance was somewhat of a surprise because of the complete absence of any external evidence of depressive affect. She was dressed neatly, in an orderly way, and with good taste. There was an accomplished use of lipstick, powder, and cosmetics, out of keeping with the affective disturbance described by the husband. She formulated the basis for her visit as follows: "I'm very much depressed since my misfortune." She described herself as lacking in ambition, avoiding people, and being especially concerned about her change in appearance. She reported circles under her eyes that she believed to be so apparent and disfiguring that she did not wish to be seen by people. She described her marriage positively, emphasizing what a wonderful person her husband was. She did mention the sexual incompatibility in essentially the same terms as the husband, but without any self-blame.

In elaboration of the history, the patient was found to be an only child. Her mother was described as a devoted, self-sacrificing woman who has made her home with her daughter since marriage. The choice of her husband was based to a large extent on his acceptance of her mother in the household. Her engagement to a more desirable suitor than the man she married was broken because of his refusal to include her mother in their marriage plans. Her father died when the patient was 9 years old. She specifically recalled a strong feeling on her father's death of not wanting to be pitied by the other children on her return to school. Her father had been disappointed in not having a son. He was described as having been a fearless cavalryman in the Russian army. The patient believed that he spoiled and indulged her with material things. During later visits material was brought forth indi-

cating the patient's fear of contamination by germs and the unusual steps she took to avoid contacts that might lead to illness.

The patient recalled her mother's stories about her having been a "colicky" baby who cried day and night until it was discovered that the mother's breast provided insufficient milk. She was always considered as "being afraid of everything" as a child. Religious practices of a highly detailed ritualistic nature were important elements in her childhood experiences. Her grandparents, who lived with her family, were orthodox Jews. Her parents, notwithstanding their Americanization in other regards, maintained all of the taboos, rituals, and prayers of very orthodox Jews. The atmosphere of the home was suffused, therefore, with countless superstitions and magical attitudes. One was constantly in a state of danger from evil spirits and impulses. Safety from sinning and avoidance of punishment was maintained by prayer and by proper observances. Wicked thoughts among the orthodox are no less reprehensible than wicked acts; unintentional sinning requires expiation and forgiveness no less than the intentional.

During the first six years of her life she slept with her parents. The development of nightmares led to their consulting a psychiatrist. The sleeping arrangements were changed. She related several childhood incidents of engagement in sex play with another girl and of voyeuristic acts. With a girl friend, she would try to watch the janitor undress to retire.

Her education was completed with graduation from high school. She always felt that she was a person of limited intelligence. In later interviews, it was revealed that she accepted a continued reference by her older cousins as being dumb. This appeared a significant determinant for her belief that she did not know as much or understand as much as her contemporaries. During her treatment, this defense of not knowing or understanding readily appeared whenever anxiety was provoked, or when an explanation for the alleged inadequacy of some item of behavior became necessary. She found employment in general office work and continued in a clerical capacity with a government agency during the first few years of her marriage. Her mother lived with them and functioned as housekeeper. There was also the desire to increase the family income. When they became financially more secure, she quit work. She experienced no significant problems in her working situation.

During the first few visits, the patient emphasized her avoidance of people. She attributed this to the alleged changes in her appearance noted 10 days after leaving the hospital. She also had begun to talk less "since it happened. What I will say will come out the wrong way." She described the disfiguring circles under her eyes and stressed her discomfort and shame at being "this way." There was a repetitive dwelling on her "misfortune" and the change that had come over her as a result of grief over her child's death.

The nature of the mental content and the discrepancy between what was being expressed and the patient's very positive appearance was quite striking. It was felt that the patient had been quite relieved to find that she was not going to have the responsibility of rearing a child. The significance of a child and of its death shortly after birth, based upon deeper dynamic factors, was not as evident as the surface dynamics, which may be described briefly as: "I'm happy that my child was born dead, but such a feeling is dreadful and shameful. How can one be happy at having one's child die?" Repression of the affect of

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elation led to a feeling that somehow the happiness showed through. The defense against this forbidden feeling was a conviction that she looked the part of a mother who has had a misfortune. The fear that she might be seen as a healthy attractive person so soon after the death of her child led to the further defenses of avoiding people and feeling that she was being talked about. The last line of defense was to avoid being seen as a person who looks radiantly beautiful after the death of a child. Instead she gratified her narcissistic need for attention and recognition through the fantasy of being talked about.

The confrontation statement was intended to unmask these defenses and arrest further development of the delusional idea of a change in body image with accompanying ideas of reference. The patient was told in a very calm, emphatic manner: "You should be the most unhappy person in the whole world because your child died! What do you think of what I told you?" The patient seemed taken aback for a moment, and then said, "I have been unhappy since it happened, but I've taken the wrong attitude. I should have thanked God for saving my life. God didn't want to give me a sick child, so he didn't give me one at all. I should have counted my blessings. I took the wrong attitude. I ran away from my responsibility to my husband and mother." The patient failed to keep her next appointment. On the following appointment she reported an improved acceptance of going into situations where she would be seen by people. When she mentioned concern about being seen by people because of her changed appearance, she was asked: "What did you think about what I told you?" The patient then related how, toward the end of her pregnancy, she began to ruminate about the great responsibility she would incur by shopping for the baby, and how she was immobilized about making decisions. She could not choose among alternatives, nor could she decide whether it was right or wrong to buy something she had in mind. Shortly after the delivery, when her husband informed her that the baby had expired, she experienced the fleeting thought: "Just as well it died." "It was horrible to think of a thing like that. From that moment, I started to punish myself for it."

In the next few visits the patient completely lost her symptoms. "I can go out and don't feel people are looking at me like a freak." She began to deal with problems preceding her pregnancy: her marked feeling of inadequacy, inability to accept responsibility, infantile sexuality, and the latent problems with her husband centering around her rejection of him. She became more accepting of him and had intercourse with him for the first time since the pregnancy began. "What should have happened in seven years took place. My husband and I had intercourse, and we both enjoyed it."

At the time this report is being written, the patient has been seen 15 times on a weekly interview basis. It would seem that the patient had been on the verge of developing a psychotic episode with a fixed somatic delusion. This malignant trend was arrested, and she was converted into a person who can work effectively in a psychotherapeutic process that will be primarily uncovering. Although the patient seems to be making strides in the direction of marked personality alteration, there is still some uncertainty of the depth of the personality change, or as to whether the change is brought about through the transference need to please and behave correctly so that she may earn approval. However, it is clear that the development of a paranoid psychotic syndrome was averted. The possi-

bility for developing personality changes in the direction of increasing the ego span has been strengthened.

Evidence of any untoward effects of the potentially traumatic nature of the confrontations, in a large number of patients, were not noted in any patient except 1. She made an abortive suicidal attempt, which did not seem genuine. Since then, even this patient has made considerable progress, not only in the decrease of symptoms over a period of several months, but also in terms of a better social adjustment. Few patients failed to return for further therapy even when such maneuvers were used in a first visit. In some patients, this technique strengthened their desire for further treatment. In still other patients, dramatic changes have occurred that seem to be other than so-called "transference cures." It is my impression that using such maneuvers in therapy may shorten the therapeutic process, an undeniably important advantage. I hesitate to suggest that this one technical psychotherapeutic device has been crucial in determining the improvements that have been noted. I am fully aware of the need for carefully controlled studies in evaluating results with psychotherapy. Appel et al⁸ have recently shown how little validated information is available on the effectiveness of any psychotherapeutic procedure, and that such statistical data as is available does not speak favorably for the value of any one technique or system of therapy over any other. There is much room, however, for first establishing some comparative measuring rod. The suggestion offered in this paper for using a statement, followed by a request that the patient explore for himself the significance of this communication, constitutes a relatively constant psychotherapeutic technique that might be especially useful in a sector type of psychotherapy or as part of the technique used in intensive uncovering therapies. The question directed at allowing the patient to tell what he thinks about the command leads to a re-exploration of past experiences and their significance to his present life. The question also points up the treatment, itself, as a means of exploring the patient's reactions to significant figures in his past.

I would also suggest that the technique described has some specific possibilities as a research technique in dealing with psychotherapeutic methods. By studying one particular statement and the patient's responses to it over a period of time, one might discover some exceedingly significant alterations in the patterning of psychodynamic material. The reactions of the patient may be considered varying responses to a fixed variable. The changing nature of the responses to such a fixed variable may enable one to gauge or estimate change in the patient through time.

RESUMEN

Se estudian en este trabajo las dificultades encontradas en el tratamiento de pacientes con ideas delirantes de tipo somático y el pronóstico relativamente malo de estos enfermos. Se describe el tratamiento favorable de una paciente que tenía la idea fija de creer que sus párpados estaban manchados. También se describe el éxito terapéutico obtenido al interrumpir el desarrollo de una idea delirante de tipo somático en su estado naciente. El delirio de esta enferma comenzó poco tiempo después de haber tenido un hijo que murió al nacer. También se expone el tratamiento psicoterápico orientado psicoanalíticamente y el uso de

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una técnica de confrontación, en la cual el centro del conflicto se presentaba repetidamente en una misma expresión verbal, no con la intención de que el paciente se dé cuenta de su estado, sino para que le constituya un estímulo en torno al cual el enfermo pueda asociar ideas y experimentar sensaciones afectivas y reacciones de transferencia. A esta paciente se le rogó constantemente que expresara sus pensamientos acerca de la expresión verbal que se le repetía. Esta técnica sugiere cómo una forma de intervención activa acelera el trabajo de penetración mental para lograr una solución socialmente más eficaz del conflicto con el cual la paciente ha estado luchando. La idea delirante de tipo somático desapareció en esta enferma después de unas pocas sesiones en las que se empleó la técnica de confrontación.

RESUME

L'auteur discute des difficultés rencontrées dans le traitement des malades présentant des hallucinations somatiques et de leur pronostic, qui est relativement mauvais. Le succès du traitement d'un cas d'obsession, où la malade croyait avoir autour des yeux des cercles de fatigue, et l'interruption du cours d'une hallucination somatique à l'état naissant sont décrits. L'hallucination a débuté peu de temps après qu'elle eût accouché d'un enfant mort dès la naissance. L'article décrit le traitement psychiatrique à orientation psychanalytique et l'emploi d'une technique de confrontation, dans laquelle le centre du conflit est présenté de façon réitérée sous forme d'une même formule verbale, non destinée à donner à la malade la capacité de comprendre la situation, mais comme stimulus favorisant l'élaboration d'associations d'idées, d'expressions affectives et de réactions de transférence. La malade est constamment priée d'exprimer ses idées à l'égard de cette formule. Cette technique est suggérée comme une forme d'intervention active qui accélère le processus de persuasion pour obtenir une solution plus satisfaisante, du point de vue social, du conflit contre lequel la malade lutta. L'hallucination somatique s'est dissipée en quelques visites quand la méthode de confrontation a été utilisée dans le traitement du cas décrit.

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A Synergistic Action of Prochlorperazine and Mepazine in Two Cases of Schizophrenia

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A combination of two ataractic agents may produce therapeutic benefit, although each drug when used alone may be of little or no value. Feldman¹ and Braun² have recently reported on the effectiveness of mepazine and chlorpromazine. We are prompted to report 2 cases of schizophrenia where a specific response to mepazine and prochlorperazine was exhibited. Other drugs and combinations of drugs were of no value. Neither mepazine nor prochlorperazine used separately was of benefit, but the use of both drugs induced remarkable remission of symptoms. Withdrawal of one drug or the other quickly resulted in a return of symptoms; restoration of the drugs was followed promptly by relief of symptoms.

CASE HISTORIES

Case 1. The patient was a 44 year old, married, retired, white man who was originally admitted to another hospital in May, 1956, for depression, and who was later transferred to the Bronx Veterans Administration Hospital in April, 1957, for insulin coma treatment. Approximately four years prior to his current hospital admission, the patient developed a severe agitated depression several days after an extramarital affair. The patient found on two occasions that he was impotent, and on one occasion he suffered premature ejaculation with his partner. Within a few days he became markedly depressed and experienced strong feelings of guilt and inadequacy, requiring hospitalization at a private sanitarium where he remained for nine months receiving intensive psychotherapy. Two weeks after his discharge from that hospital, he reverted to a depressed state with prolonged and frequent crying spells.

For the next year and a half, he received private psychotherapy and electroconvulsive therapy, with a slight diminution of his depression, but he became more fearful and agitated. After his doctor became ill, the patient was again admitted to a hospital. While there, he received 1200 mg. of chlorpromazine daily for two months, then 10 pentylenetetrazol convulsive treatments, followed by 6400 mg. of meprobamate daily for three weeks, and again a combined amount of chlorpromazine and meprobamate in the afore-mentioned doses daily for a period of six months. There were no noticeable results after many months on this drug therapy. The patient was then placed on 1 mg. of reserpine daily. He was then given 61 carbon dioxide treatments over a period of two months, followed by a month and a half of subcoma insulin treatments. Finally he was placed on 1250 mg. of promazine daily for two months, all without effect. Throughout this time the patient was markedly agitated and depressed, and there was a steady decline in his condition. He was finally admitted to the Bronx Veterans Administration Hospital for insulin coma therapy with a recommendation that psychosurgery be considered if shock treatment failed to improve his condition.

On admission to this hospital, however, the patient refused both insulin and surgical procedures. His illness in this hospital was characterized by obsessive ruminations, which were primarily sexual in nature, and which usually included thoughts of having oral-genital contact with members of both sexes as well as with children and adults. He felt guilty whenever he thought of having regular heterosexual relations even with his wife. He was plagued with a fear that he might be homosexual and was preoccupied with the thought that something was biting at his penis and also with the desire to crawl into his mother's lap and nurse at

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her breast. At times he was convinced that his symptoms were caused by God. He also had the feeling that he had had sexual intercourse at one time with his mother and that he had killed his father. He had the compulsion to carry out degrading acts, such as drinking urine and putting ashes in his drinking water, but never acted upon these compulsions. He had a feeling that he wanted to take his fork and plunge it into his throat. There were also occasions when he felt he would like to strike his head against the wall. He never carried out any of these acts.

In this hospital admission, the patient was placed on chlorpromazine, up to 1000 mg. daily for four months, without any effect. He was then placed on reserpine, 5 mg. daily intramuscularly, which sent him into agitated depression after two days, necessitating withdrawal of the drug. He was seen in psychotherapy with some improvement. He was then placed on perphenazine, up to 32 mg. daily for one month, with no effect. He was also placed on a trial of meprobamate again, 1600 mg. daily for a two week period, with no effect. A combination of 300 mg. of chlorpromazine and 200 mg. of mepazine daily was instituted, with some improvement over a period of one month. The patient was then placed on prochlorperazine, 20 mg. four times a day, for a period of two weeks with no improvement and an increase in agitation. He was then placed on a combination of mepazine, 50 mg. four times a day, and prochlorperazine, 10 mg. four times a day, with a marked improvement in his symptoms in only one week's time. His obsessions and compulsions diminished greatly, and overt signs of his psychosis gradually disappeared. His reality testing became excellent. The prochlorperazine was stopped, and he was continued on mepazine alone; he suffered a relapse to his old state in a matter of three days. He was restored to the combined mepazine and prochlorperazine again with a prompt remission of symptoms after three days.

The patient described his former ruminations about homosexuality and his feelings toward his mother and toward his father as all being "silly." He made an excellent adjustment on the combined drugs, and it was felt after approximately two months' treatment that he should be transferred to an open ward.

Case 2. The patient was a 40 year old, unmarried, white man who had been seen in psychotherapy for two years following a paranoid schizophrenic episode necessitating hospitalization from January, 1956, to June, 1956. The episode was characterized by severe anxiety and an elaborate paranoid delusional system, involving telephone tapping, television, and radio, attempts by his mother to poison him, and automobiles following him. He was delusionally convinced that he was being called a homosexual.

Physiological therapy administered at the time consisted of 56 insulin coma treatments and five combined electroconvulsive therapy and insulin coma treatments. He was seen in psychotherapy five times weekly, with the development of a good rapport. As he improved symptomatically on physiological therapy, he was weaned to a once a week schedule of psychotherapy and then, after hospital discharge in June, 1956, was seen on a once a week basis as an outpatient.

The patient has been employed for the past two years as an assistant engineer in an electronic plant. He now has an apartment of his own and is in a healthy relationship with a woman. He had never held a job this long before, nor had he been able to relate to a woman before or even maintain his own home before the institution of therapy. During the past two years, he has had bouts of anxiety relating to his status in the office, the criticism of his inability to relate warmly to his fellow employees, and evaluation of his performance by others.

Treatments during the acute anxiety episodes included chlorpromazine, 100 mg. twice a day, and promazine, 100 mg. twice a day. Meprobamate, 400 mg. four times a day, was tried on occasion with poor results. When the patient's capacity to ascertain what was happening to him was severely impaired, careful analysis of the situation with elucidation of the projective way in which the patient organized experience was successful. Direct advice upon prescribed issues was also employed. The above regime was successful with the patient developing a good work record and increased confidence in his capacity to withstand stress.

In March, 1958, the word began to spread in the patient's office that layoffs due to the economic recession were imminent. Fellow employees were being discharged at this time. The patient began to develop severe anxiety. He became hypersensitive to any implied criticism of his work, resulting in emotional outbursts with his supervisor. Within two weeks, he became convinced that he was in danger of being discharged and that the employees around him were talking about him and criticizing him. These thoughts were accompanied

by depression. He withdrew from contacts within the office and found himself elaborating a fantasy in which there was a master plan, involving the therapist, the supervisor, and numerous other aspects of his life experience, that was acting to direct him. He first felt that this fantasy was not true, but he later found himself unable to prevent himself from believing its reality. He noted that he had begun to respond to directives from this master plan. The fantasy became overpowering to him. He was then switched from an ineffectual regime of promazine, 200 mg. four times a day, to a combination of prochlorperazine, 15 mg. twice a day, and mepazine, 15 mg. twice a day. Within 24 hours, there was a marked diminution of anxiety with the lifting of the fantasy. This improvement was maintained for one week with a return of effectual performance at work. Because of some drowsiness, the prochlorperazine was withdrawn after one week. Within 12 hours the entire fantasy returned with the same force. Two days later, the prochlorperazine was restored, with a return of the symptomatic improvement that was maintained until the next week. At that time the patient ran out of his supply of mepazine, and a recurrence of symptomatology took place. With a reinstitution of the aforementioned regime of prochlorperazine and mepazine together, improvement occurred again. Within a month, the patient received confirmation of his job status, and the former equilibrium was re-established in the various areas of his function. He was then withdrawn from the drugs and has shown no further delusional symptomatology to date.

SUMMARY

Two cases of schizophrenia are presented in which severe psychotic symptomatology was controlled with a combination of mepazine and prochlorperazine, where neither drug alone was effective, and where other ataractic drugs had been ineffectual.

RESUMEN

Se presentan dos casos de esquizofrenia en los cuales se logró dominar la sintomatología psicótica grave con una combinación de mepazina y procloroperazina. En estos casos no había sido eficaz ninguna de las dos drogas solas, ni otros de los atarácticos empleados.

RESUME

Présentation de deux cas de schizophrénie dans lesquels la symptomatologie psychotique, qui était grave, a été contrôlée par l'association mépazine-prochlorpérazine alors que ni l'une ni l'autre de ces deux drogues administrées séparément n'était efficace; les autres ataractiques avaient été également dépourvus d'efficacité.

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Follow-up Evaluation on a Controlled, Blind Study of Effects of Chlorpromazine on Psychotic Behavior*

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Chlorpromazine has been used in the treatment of mental disorders in this country since 1953. Since that time, large groups of patients with varying degrees of mental illness have been treated with the drug. It is now possible to arrive at a more objective impression of the use and effectiveness of the drug by re-evaluating the patients who have received it.

It is well known that much interest in and enthusiasm for the ataraxics have been expressed. Since optimism about chlorpromazine parallels the introduction of other new treatment modalities, a careful evaluation of the effectiveness of this drug would be useful. Thus, it may be easier to determine the place that the "tranquilizing drugs" should have in the psychiatrist's armamentarium.

This paper will consist of a review of pertinent literature concerning the use of chlorpromazine, a brief condensation of the original study upon which this investigation is based, and finally the methodology, results, and discussion of the findings of the present research. Clinical summaries of the patients utilized in this investigation will also be presented.

REVIEW OF THE LITERATURE

The literature on chlorpromazine is quite voluminous, and no attempt will be made to review it completely. The author would like instead to present a brief, but comprehensive, view of chlorpromazine in the treatment of the mentally ill.

One cannot generalize on the over-all response of patients to the drug since there are many factors to be considered.

There was an over-all agreement that the age of the patient does not influence his response to the drug.^{1, 14, 49, 53}

The chronicity of the illness was highly correlated with a longer treatment program, higher dosages of chlorpromazine, and a lower percentage of clinical improvements. The reverse was true of acute illness with short duration.^{1, 11, 14, 16, 19-32, 56}

The medication was administered orally, intramuscularly, or intravenously. Routinely, it was given orally in divided doses. In acutely disturbed patients, the intramuscular or intravenous route was most efficacious. The dosage was individualized, but most patients were found to have a therapeutic response to 200 to 400 mg. daily.^{6, 11, 14, 31, 32, 37, 56} Larger doses were advocated by a few authors.^{16, 26, 35, 49}

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* This is a follow-up evaluation on a paper by P. E. Feldman, et al.¹³

Tenment⁵³ emphasized that in aged people who are feeble, one should start off with an initial dose of 25 mg. and increase it slowly.

Feldman¹⁵ found that prolonged administration of chlorpromazine did not lead to tolerance formation, and maintenance dosages were substantially smaller than the dosages necessary to obtain the initial therapeutic response.

Maintenance therapy was continued indefinitely unless the basic pathology was altered. A certain percentage of patients who lived successfully and had a real ego reorganization on this basis could in time be taken off the drug.⁵⁶

Relapse rate after withdrawal of the drug was 80 per cent in six months. This rate was markedly reduced if the patients were also being treated by psychotherapy.⁵⁶

Feldman,¹⁵ in a two year fate study of 317 patients, found that 65.5 per cent who were still in the hospital were receiving chlorpromazine. Ninety-six of these patients (26.2 per cent) who were released from the hospital were on maintenance dosage of the drug.

Pollack^{42, 43} emphasized the continued use of a maintenance dosage of chlorpromazine following release from the hospital. He found that it reduced the relapse rate from the expected 35 per cent to 5 to 7 per cent.

Pollack⁴² stated that there are four purposes in giving maintenance doses of chlorpromazine: (1) To control or modify the emotional, psychic, and behavioral disturbances in a person still mentally ill but improved, (2) to prevent relapses in an apparently recovered person, (3) to modify or change the personality reaction of the individual to the realistic demands of everyday life, and (4) to improve receptivity of the patients and aid in continued psychotherapy.

Chlorpromazine found its greatest usefulness in relieving or diminishing certain symptoms found in mental illness. Those for whom it was most effective were patients with anxiety, psychomotor excitation, delusions, and hallucinations, as well as those with various behavior traits related to these, such as agitation, tenseness, violence, assaultiveness, hostility, panic, confusion, destructiveness, denudativeness, smearing, and soiling.^{5, 8, 9, 14, 16, 17, 28, 29, 31, 35, 37, 48, 50, 53, 56} Chlorpromazine was found to be of little help with such symptoms as depression, obsessions, and severe apathy and autism.^{6, 9, 35, 50, 56}

In the treatment of the neurotic patient, chlorpromazine was only of limited usefulness. It was used as an adjunct to psychotherapy when there was considerable anxiety, but its role was definitely secondary.⁵⁶ When the drug was used as the only method of treatment, the results were poor.^{14, 16, 28, 35, 37}

Chlorpromazine has found its greatest usefulness in the treatment program of the psychotic patient. The majority of the patients who have been studied in the mental hospitals were diagnosed as schizophrenic. Freeman,¹⁶ in a review of the literature concerning treatment of schizophrenic patients, found that the following percentage was discharged from mental hospitals to the community in a condition approximating that observed before they became ill: From a group of 11,080 schizophrenic patients with varying periods in the hospital, complete and social recovery was obtained in 19 per cent. This figure must serve as the base line against which all other methods of therapy should be compared. In 7357 schizophrenic patients treated with convulsive shock therapy, the rate of complete and

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social recovery was found to be 29 per cent. In 9483 schizophrenic patients treated by the insulin coma technique, 48 per cent recovered. In 1211 patients treated with lobotomy, the value was 18 per cent. For 1517 cases treated with chlorpromazine, the figure was 34 per cent and for 897 patients treated with reserpine, the figure was 22 per cent.

Feldman,¹⁴ in his study of 238 schizophrenic patients, found that 9 per cent achieved marked improvement, 25.5 per cent moderate to marked improvement, and 17.5 per cent moderate improvement, with a total of 124 patients (52 per cent) showing a moderate to marked improvement as a result of chlorpromazine therapy. Patients with paranoid or catatonic reactions responded best, with 59.5 per cent showing moderate and 56.0 per cent marked improvement. He found that hebephrenic and undifferentiated reactions were benefited to a lesser degree. The 10 patients with a schizoaffective reaction comprised too small a group to warrant any generalizations, but over half were markedly improved.

The findings of greatest clinical improvement in paranoid, catatonic, and schizoaffective reactions and least improvement in simple and hebephrenic reactions were confirmed by a number of studies.^{19, 26, 41, 42, 48, 58}

Winkelman⁵⁶ found, in his study of 130 schizophrenic patients, that 19 per cent became symptom-free, 61 per cent obtained moderate or better results, and 22 per cent failed to respond.

Kinross-Wright,²⁶ in a study of 108 schizophrenics, obtained complete or social remissions in 76 per cent. He obtained also a higher percentage of improvement in the hebephrenic and chronic undifferentiated group.

One of the most effective uses of the drug was in the treatment of manic depressive psychosis, manic type.^{9, 19, 30} Greater than 50 per cent recovery was reported by authors who have treated patients in the manic phase.^{1, 14, 16, 28}

For psychotic depressions, drugs were of little value and electroshock therapy was the treatment of choice.^{16, 48, 56}

In the involutional psychotic reactions¹⁴ and psychotic reactions of the aged^{16, 53} the results with chlorpromazine have been extremely good, with improvements in the range of 75 per cent. It was particularly helpful when agitation, irritability, and psychomotor excitement were present.

In acute alcoholism, chlorpromazine was quite helpful.^{1, 9, 16, 28, 30} In chronic alcoholism, the drug relieved the anxiety but did not prevent the patients from drinking.¹⁶

A study of the effectiveness of chlorpromazine on the organic brain syndrome was reported by Feldman.¹⁴ In senile, arteriosclerotic, and other types, he found that 44, 62.5, and 32.0 per cent showed marked to moderate improvement, respectively. A number of the patients showed surprising improvement in areas such as memory, judgment, and orientation, as well as destructiveness, excitement, and confusion. Similar favorable results have been reported by Denber and Bird.¹¹

The most common side effect was drowsiness, which was seen in 22.8 per cent of the patients treated in the Feldman study.¹⁴ Other reactions, such as parkinsonism, skin rash, and dizziness, were each found in less than 4 per cent of all the patients. The incidence of jaundice was only 1.9 per cent, blood change 1.9 per cent, and hypotension 2.8 per cent.

Other studies on side effects correlated well with the findings described and indicate that they are fairly infrequent and not serious.^{6, 9-11, 16, 26, 28, 32, 35, 39, 53, 56}

Belisle et al³ found that the drug increased the patient's ability to respond to the milieu and auxiliary therapies. The use of drug therapy created an atmosphere that allowed improvement of severely regressed patients who had received none of the drug.

Lesse³³ reported on the use of chlorpromazine and analytically oriented psychotherapy in the treatment of 100 patients. The age range was 15 to 60 years and the average 35 years. There were 44 psychoneurotics, 42 schizophrenics, and 14 involutional psychotics. The combined treatment lasted from three to six months.

Chlorpromazine primarily acted to decrease overt anxiety in the three phases of therapy: (1) Early in treatment it hastened "anxiety decompression"; the subsequent positive transference was stronger than would have been expected without the drug. Negative transferences were blunted and carried less emotional impact. (2) During the course of psychotherapy, it alleviated the mounting anxiety that insights gained through therapy often precipitated. The drug was effective in avoiding schizophrenic panic. The changes in patient-doctor relationships were relatively mild and did not obstruct the therapeutic process. (3) Chlorpromazine increased the production of dreams in more than one half the cases where overt anxiety was present. When anxiety decreased, the manifest content of dreams changed.

Chlorpromazine was effective in about one third of the severely agitated depressed patients; if they manifested suicidal trend, the drug was contraindicated. Giving chlorpromazine would greatly increase the number of patients, particularly schizophrenics, who would be available for psychotherapy in an office or on an outpatient basis.

The role of chlorpromazine in individual and group psychotherapy is at present being evaluated. The combination of chlorpromazine and psychotherapy seemed to offer the greatest opportunities for the patient with sufficient ego strength to reduce his intense preoccupations and rapidly form a relationship with a psychotherapist.^{5, 7, 26, 40, 46, 56}

Unresolved conflicts are manifested as anxiety, and anxiety in turn is the prime force in the development of psychiatric symptoms. Chlorpromazine appeared to affect most favorably those patients whose symptoms were manifested by anxiety. The drug reduced the anxiety and the symptoms. It would seem that the id impulses and superego rigidity were likewise reduced, thus allowing the ego to function more smoothly and effectively. Since the ego had fewer conflicts to handle, it was relatively strengthened. This allowed an opportunity to reintegrate on a higher level of functioning. In most instances, when the drug was discontinued the anxiety and symptoms recurred unless intensive psychotherapy was instituted and the patient was able to make some basic readjustments to his personal problems by this means. Thus it is important to realize that the drug offers symptomatic relief and is not in itself curative.^{51, 56}

The pharmacological action of chlorpromazine was presented in a detailed study by Rinaldi and Himwich.⁴⁷ They found that chlorpromazine is a depressant of the mesodiencephalic activating system and a good sedative that relieves anxiety. The drug also produces autonomic changes that are partially due to a peripheral effect. It has an adrena-

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lytic action, blocking the depressor and hyperglycemic effects of epinephrine. It has a ganglionic blocking property and also an atropine-like effect.

Chlorpromazine has a depressant effect on the central nervous system. It produces a fall of body temperature and a decrease of the metabolic rate. These changes indicate that the drug exerts a restraining action upon the hypothalamus. It has other central nervous system effects of a depressant type including the potentiation of the actions of narcotics such as barbiturates.

Chlorpromazine inhibits the hypothalamus and thus produces therapeutic reduction of anxiety. The sedative action of the drug is probably related to the depression of the hypothalamus and in larger doses to that of the mesodiencephalic activating system.

The depression of the hypothalamus also withdraws support from the anterior pituitary and alters the endocrine balance. It depresses the reticular formation that functions in the alerting reaction.²¹

INITIAL STUDY

From December, 1954, until February, 1955, Feldman et al¹³ conducted an investigation concerning the effects of chlorpromazine on psychotic behavior. Twenty-two male patients from Topeka State Hospital, Topeks, Kan., were selected at random as subjects for this experiment. Most of these patients were considered to be management problems by the staff, but no attention was paid to their diagnosis, age, chronicity of illness, nor to the course of illness. These subjects were divided into two groups of 11 with an attempt being made to cross-match the patients according to their diagnostic category.

For the first three weeks both groups received placebo medication. The experimental group was then placed on chlorpromazine for three months while the control group was continued on placebos. Four psychiatrically trained raters evaluated the patients during this period on a seven-point clinical scale, and Fergerson Hospital Adjustment ratings were computed at various times during the study.

The results of this study were that on clinical ratings 9 out of 11 of the patients receiving chlorpromazine improved, whereas only 4 of the placebo patients improved. It was pointed out that this difference in improvement in the two groups is statistically significant. Even though all the requirements for the correlation technique employed could not be met, it was found that the clinical raters rated in a consistent manner. The Fergerson rating scale proved to be disappointing in that a statistically significant difference between the groups was not found.

In their discussion, the authors point out that the average duration of illness for the 9 patients receiving chlorpromazine who improved was 18 years, whereas the 4 improved patients on the placebo had been ill for a much briefer time. It was felt that the results of this study could not be explained on the basis of suggestion or an accelerated milieu program.

The final conclusions of this study were: "In our experience, Thorazine is a useful addition to the armamentarium of the psychiatrist and it can at times produce dramatic improvements in cases that have been completely refractory to other forms of somatic therapy.

KILGORE

Thorazine was found to be useful in converting acutely disturbed psychotics into tractable, accessible patients who could then participate more actively in the hospital rehabilitation program."

PRESENT STUDY

It is noted that two and one-half years after the initial study, 10 of the 11 original patients treated with chlorpromazine are still in the hospital. Since so much has been published concerning patient improvement on the drug, it seemed that a follow-up study on these patients might prove interesting. It would not be fruitful to study Feldman's placebo group because most of these patients have been placed on one of the ataractic drugs during this two and one-half year period.

Methodology. Subjects utilized in this study are 10 of the original 11 patients in Feldman's chlorpromazine group, all of whom are still hospitalized at Topeka State Hospital. The two methods used to evaluate what changes, if any, have occurred during the two and one-half years since the completion of Feldman's study are clinical ratings and the Fergerson Hospital Adjustment Scale. The last Fergerson ratings completed in the previous investigation are compared with ones tabulated at the present time.

The Fergerson Scale consists of part I (Communication and Interpersonal Relationships), part II (Care of Self and Personal Appearance), part III (Work, Activities, and Recreation), and total (Total Hospital Adjustment).

Three well-trained clinical raters independently ranked the 10 experimental patients on a 10 point scale, assigning a score of 10 to the patients with the best present adjustment down to a rating of 1 for the patient with the worst present adjustment. Since all three of the clinical raters had access to the previous notes on each patient, it was possible for them to rate independently each of the 10 experimental patients on a 7 point scale in terms of degree of change of adjustment over a two and one-half year period. This scale consisted of the following levels: (1) Condition aggravated, (2) condition unchanged, (3) mild improvement, (4) moderate improvement, (5) moderate to marked improvement, (6) marked improvement, (7) striking improvement.

Results. Utilizing the binomial method of significance of change, it was found that none of the four Fergerson measures showed a significant change over the two and one-half year time period.

By use of coefficients of concordance it was determined that the clinical raters agreed to a highly significant degree ($W = 0.97, p < 0.01$) in their clinical ratings of the patients on the 10 point scale. Similar consistency was found for the raters on the 7 point scale ($W = 0.90, p < 0.01$).

In order to determine if the Fergerson ratings of present total adjustment agreed with the clinical ratings of present total adjustment, it was necessary to compute an average of the ratings of the three raters. By the use of a τ coefficient it was found that the Fergerson present adjustment ratings were significantly correlated with the average clinical present adjustment ratings ($\tau = 0.69, p < 0.01$).

The binomial method of determining significance of change was employed in order to

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determine if there was a significant change in adjustment over the past two and one-half years as measured by clinical ratings. Averages of the clinical ratings on the previously mentioned 7 point scale were found, with the justification for this method again being the high agreement of the raters. It was found that there was no significance of change for the 10 patients in the experimental group.

DISCUSSION

The results of the new study indicate that the experimental group of 10 patients was able to maintain the initial improvements noted in the Feldman study, but that there had been no additional significant change of adjustment either on any part of the Fergerson scale or on the clinical ratings during a period of two and one-half years. Taken at face value, this would indicate that chlorpromazine is not effective in terms of further improving the total hospital adjustment of these 10 experimental subjects.

However, a closer inspection of the individual patients indicates that some of them improved remarkably either in terms of leaving the hospital for trial visits or of being sent to an open ward. Also 1 of the original patients in the chlorpromazine group could not be included in this study because he was able to leave the hospital.

Although it is possible that these individual cases of striking improvement might be due to chance factors, it could also be that the lack of homogeneity of this particular group in terms of age, intelligence, education, chronicity, and type of illness might account in part for these negative results. Since all of these factors influencing homogeneity have been cited in the literature^{20, 22, 23, 44, 45, 52, 57} as being important in clinical research, the question of the effectiveness of chlorpromazine must still be considered to be open. Further research taking the factors influencing homogeneity into consideration might be worth while.

Other results found, which might be of importance for further research, are that well-trained clinical raters are able to rate in a consistent fashion, and that the Fergerson Scale and clinical ratings are significantly similar.

CLINICAL SUMMARIES

Case 1. F. D., a 20 year old boy, was admitted to Topeka State Hospital on March 16, 1954, because of a sudden onset of a catatonic stupor. He had received 12 electroconvulsive treatments by July, 1954, and had made some improvement. In November, 1954, at the beginning of the Feldman study, he was described as alert and in good contact. His answers to questions were goal-directed, but accompanied by a silly inappropriate smile. He expressed no unusual ideation, though his thought content indicated preoccupation with violence and aggressive acts. His behavior was characterized by frequent episodes of combativeness and excessive teasing of other patients. At times, he became quite noisy and hostile toward the personnel. He received 400 mg. of chlorpromazine per day during the study.

At the conclusion of the Feldman study in February, 1955, it was reported that he continued to be provocative, argumentative, and demanding. At times, he was restless and fearful and engaged in many altercations. His clinical evaluation at that time indicated a slight improvement.

During the past two and one-half years, the patient has made steady improvement. His chlorpromazine dosages have been as much as 1000 mg./day, but at present he is on 200 mg./day. He has been in group psychotherapy for two years, and he has regarded this as a quite meaningful experience. He was able to enter into a very active milieu program. He began to assume more responsibility for himself, becoming less childlike, dependent, and demanding. He was then able to have weekend passes to see his parents, who were helped

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through casework to relate to their son in a more meaningful way. It was then possible for the patient to verbalize and discuss some of his fears and insecurities in a way that was helpful to him. On his own initiative, he was able to make plans and attend one course in summer school. At this time he became more openly demanding, dependent, and insecure, but with support he was able to verbalize his fears and get help from the ward physician. He made a grade of B in his English course and was quite pleased, although he had the feeling he should have done better.

Following summer school, he went on a vacation with his family. In September, 1957, he started to school on a half-time basis and was transferred to an open ward. He has been rated as having markedly improved during the past two and one-half years. He was rated first with regard to the group adjustment.

Case 2. R. M., a 33 year old man, was admitted to Topeka State Hospital on February 27, 1953, with a diagnosis of schizophrenic reaction, paranoid type. He had received 79 insulin coma treatments during his hospitalization, with slight and temporary improvement.

In November, 1954, at the beginning of the Feldman study, he was described as extremely regressed, disheveled, and disinterested in his surroundings. He was poorly oriented as to time, and his memory was hazy for recent and remote events. He was delusional, occasionally combative, and his mood was inappropriate.

In February, 1955, he was rated as having made marked improvement. The delusional material was now at a minimum, and he seemed in very good contact. He became active in occupational therapy, concerned about his appearance, and was pleasant and smiling. He wrote sensible letters home and formulated plans for his release.

The patient had three trial visits home, at all of which he did well. In July, 1955, he eloped, as he was impatient with parole plans. Following this, he was paroled. While out of the hospital, he did not continue his medication, and there was a recurrence of earlier symptoms. He was readmitted in January, 1956. It was decided to see what response mepazine would produce on the patient's symptoms since this drug was under study at that time. There was no improvement, mepazine was discontinued, and he was started on chlorpromazine again in June, 1956. There was a dramatic improvement of his symptoms. He was then able to participate actively in a milieu program and soon after that to have an industrial assignment.

In September, 1957, he was paroled. The plan was that he would live at home, find work in the community, and continue on a maintenance dosage of chlorpromazine.

He was rated as having made a moderate to a marked improvement. He was rated second with regard to his group adjustment.

Case 3. W. G., a 44 year old man, was first admitted to Topeka State Hospital on June 29, 1946. His diagnosis was schizophrenic reaction, paranoid type. He received two courses of insulin coma therapy with improvement that was not maintained.

In November, 1954, at the beginning of the Feldman study, the patient was described as tense, suspicious, and evasive. He was a victim of many delusions. He usually sat quietly on the ward, but occasionally he would burst out with inappropriate laughter. He participated passively in adjunctive therapy. He was placed on 200 mg. of chlorpromazine daily.

In February, 1955, he was rated as having made a moderate improvement. He was able to get along well with the other patients and ward personnel. He appeared to be without suspicions. He was tolerant of provocative behavior from others. His replies to questions indicated realistic thinking. His mood and responses were more appropriate.

The patient continued to improve until he was able to go home on weekend passes. He made plans to leave the hospital and obtained employment in his home town before his parole on October, 1955. It was recommended that the patient continue on a maintenance dose of chlorpromazine.

He was returned from parole in August, 1956, with much the same symptomatology as before. He had not continued his chlorpromazine on leaving the hospital. Chlorpromazine medication (300 mg. daily) was re-instituted along with an active milieu program. The patient made a rapid symptomatic improvement. He is described now as compliant, cooperative, and pleasant. There is emotional blandness. There has been no evidence of delusional thinking. He has a job in the pathology laboratory as well as an active milieu program.

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This patient has been rated as having made a slight to moderate improvement. It was felt that he was third with regard to the group adjustment.

Case 4. H. B., a 49 year old man, was admitted to Topeka State Hospital on August 18, 1948, with a diagnosis of schizophrenic reaction, paranoid type. He had a lobotomy in 1950.

In November, 1954, at the beginning of the Feldman study, he was described as being somewhat apprehensive but cooperative and compliant. His conversation was primarily coherent and goal-directed and his orientation was adequate, but his memory was hazy for some remote events. His behavior was characterized by emotional lability, excessive demands, and brief outbursts of rage when frustrated. He expressed no delusions. He was placed on 200 mg. of chlorpromazine daily.

In February, 1955, he was rated as having made slight improvement. The most striking change noted was his increased ability to get along with the other patients on the ward. He was less irritable, and he had few temper outbursts. He was more at ease during interviews and smiled a great deal. He became more active in participating in occupational therapy and social events.

The patient continued to make some improvement in his ability to relate to the patients and personnel. During the past two years, he has been able to have an off-ward industrial assignment as well as a ground pass, which he has handled well.

In November, 1956, mepazine was added to his treatment program. Because of the patient's occasional violent temper outbursts, he has been receiving 1200 mg. of chlorpromazine and 600 mg. of mepazine daily.

The patient has been rated as having made a slight improvement. It was felt that he was fourth with regard to the group adjustment.

Case 5. L. M., a 33 year old Negro man, was admitted to Topeka State Hospital on October 6, 1949, with a diagnosis of schizophrenic reaction, catatonic type. He had received a course of electroconvulsive therapy prior to July, 1953, without benefit. He also received subcoma insulin therapy in July, 1954, without change.

In November, 1954, at the beginning of the Feldman study, he was described as mute, sullen, glaring at everyone. Occasionally he uttered a monosyllabic response. He was tense and extremely hostile, disheveled and untidy in his personal habits. Frequently he paced up and down the ward, but avoided contact with others. He appeared to be actively hallucinating. He was placed on 200 mg. of chlorpromazine daily.

In February, 1955, he was much less hostile and more compliant and cooperative. His ward adjustment was good, and he was actively entering into occupational and music therapy. He began to participate spontaneously in the ward meetings. His clinical evaluation at that time was one of moderate to marked improvement.

The patient was described as continuing to make improvement in his thinking, behavior, and actions. In October, 1955, he developed swelling of the gums, loss of appetite, and increased salivation, and the drug was discontinued. His earlier symptoms began to recur in about six weeks, the drug was reinstated, and he again made a symptomatic improvement.

Following this, azacyclonol was added to the treatment program, since this drug was under study at the time. There was no change noted that could be attributed to the use of azacyclonol so it was discontinued after six months.

The patient has a warm friendly teasing way about him that can change to one of hostility without great provocation. He has been able to help plan and make several three day visits home. He has actively participated in his milieu program. His present chlorpromazine dosage is 300 mg. daily.

He has been rated as having made slight to moderate improvement. He was rated fifth with regard to his group adjustment.

Case 6. H. A., a 44 year old man, was admitted to Topeka State Hospital on February 20, 1940, with a diagnosis of schizophrenic reaction, paranoid type with catatonic features. He received subcoma insulin therapy in July, 1954, without improvement.

In November, 1954, at the beginning of the Feldman study, the patient was described as being untidy, displaying little interest in his surroundings, and having periods of overactivity and combativeness. He re-

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mained aloof from other patients. Occasionally, he smiled in a silly, inappropriate manner. He had delusions of being an actor and going to Hollywood. He was well oriented, and there was no gross evidence of a memory disturbance. He took no part in adjunctive therapy. He was placed on 200 mg. of chlorpromazine daily.

In February, 1955, the patient was rated as having made marked improvement. He became much more sociable and friendly. He made some close friendships with other patients, and he related well to all the ward personnel. He actively participated in occupational therapy and ward work. His hyperactivity and combativeness subsided completely. His mannerisms diminished. He verbalized the same delusions but expressed them without emotions or convictions.

During the past two and one-half years, the patient has had several periods during which he relapsed and exhibited his earlier symptoms. This occurred while he was receiving chlorpromazine and when there were no external precipitating causes known by the personnel. On one occasion he received as much as 1600 mg. of chlorpromazine daily. At present, his medication is 300 mg. daily. The patient was doing well in regard to his ward adjustment and in his relationships with the ward personnel. He requested an industrial assignment, and this was arranged. He did well on this assignment for the next six weeks. It was decided that he could make a satisfactory adjustment on an open ward with additional responsibilities. However, about one week after the transfer he became more withdrawn and mute and refused to go to work. He indicated he wanted to return to his former ward, and this was permitted.

This patient was rated as having made a slight improvement. He was rated sixth with regard to his group adjustment.

Case 7. G. F., a 58 year old man, was admitted to Topeka State Hospital on January 16, 1926, with a diagnosis of schizophrenic reaction, hebephrenic type. He had not received somatic therapy prior to the Feldman study.

In November, 1954, at the beginning of the Feldman study, the patient was described as slovenly and untidy, and appeared older than his years. He frequently paced about, muttering incomprehensibly to himself. He was not a major problem in management, but he was moderately negativistic. He responded to questions with an aggressive tirade containing much symbolic and delusional material. Occasionally, he had outbursts of violent anger. He was placed on 200 mg. of chlorpromazine daily.

In February, 1955, he was rated as having made moderate improvement. He was neater and cleaner in dress and appearance. He was much quieter and less verbally aggressive. His conversation was more realistic and contained little delusional material. His hallucinations became minimal. He made an excellent ward adjustment and participated actively in occupational therapy and ward work.

During the past two and one-half years, there has been essentially no change from his condition in 1955. He has received up to 2000 mg. daily of chlorpromazine. He was given chlorpromazine combined with reserpine for a period of three months when this drug was being investigated, without noticeable change. He now receives 300 mg. of chlorpromazine daily.

The patient has been rated as having shown no change. He was rated seventh with regard to the group adjustment.

Case 8. C. M., a 52 year old man, was admitted to Topeka State Hospital on May 16, 1947. His history indicated he had encephalitis in 1931, which was followed in a few years by grand mal convulsive seizures. At the time of admission, his diagnosis was chronic brain syndrome with psychosis.

In November, 1954, at the beginning of the Feldman study, he was described as having cycles of overactivity, overtalkativeness, extremely paranoid thinking, and explosive outbursts of hostility and combativeness. He was prone to complain of many somatic ailments. He averaged one grand mal seizure every 7 to 10 days. He was placed on 200 mg. of chlorpromazine daily.

In February, 1955, at the conclusion of the Feldman study, the patient was described as being pleasant and affable. He was better able to tolerate frustration and was more alert. He was able to make a satisfactory visit home and had had only one seizure during the previous three months. He was more cooperative and less agitated and complaining. It was felt that he had made a moderate to a marked improvement.

He seemed to get a great deal of satisfaction from his ward housekeeping assignments. He was able to handle

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a ground pass, and there was seldom evidence of aggressive outburst. He was able to make three trial visits home. At times, he hid his medication rather than taking it. Since he was doing so well, he was transferred to an open ward.

He seemed to have more than the usual difficulties in changing from one ward physician to another. When one physician left with whom he had a close relationship, the patient began to talk more about his civil rights. He found fault with the new physician and other patients. He expressed paranoid ideation.

It was necessary to transfer him back to the closed ward. With the additional security, the patient was able to rapidly reconstitute to his former level of adjustment. This sequence of events has occurred several times during the past two years.

He was rated as having remained unchanged since the termination of the Feldman study. He was rated eighth with regard to the group adjustment.

Case 9. L. G., a 51 year old man, was admitted to Topeka State Hospital on June 30, 1938, with a diagnosis of chronic brain syndrome with psychosis (paresis). He had received fever therapy (malaria) and antiluetic therapy without benefit.

In November, 1954, at the beginning of the Feldman study, he was described as quiet, cooperative, and pleasant. He was aphasic and incapable of uttering more than unintelligible sounds. He worked regularly in the kitchen and presented no problems in management. He had good contact with his environment. He comprehended questions and instructions and was able to communicate his wishes by writing. He was placed on 200 mg. of chlorpromazine.

In February, 1955, it was concluded that he showed no change.

Since the patient made no response to chlorpromazine, it was discontinued. Following this, he had a trial on chlorpromazine combined with reserpine and later on meprobamate with no improvement.

The patient at present is on no medication. There has been no essential change noted from that described above. He does participate on an inpatient activity program.

He has been rated as having shown no response. He was rated ninth with regard to group adjustment.

Case 10. H. O., a 37 year old man, was admitted to Topeka State Hospital on May 13, 1941. His diagnosis is schizophrenic reaction, hebephrenic type. He had received no somatic therapy prior to the Feldman study.

In November, 1954, at the beginning of the Feldman study, he was described as being sloppily attired and untidy in his personal habits. He was preoccupied with senseless diagrams and mazes. His speech was primarily symbolic, usually incoherent, and accompanied by an inappropriate smile. Occasionally he participated passively in ward activities, but his interest was not sustained. Frequently he lay down in the day room or in the bathroom. He was placed on 200 mg. of chlorpromazine per day.

In February, 1955, at the conclusion of the study it was felt he had made slight to moderate improvement. He was more friendly and alert. He began participating actively in adjunctive therapy and responded to questions in a more coherent and relevant way.

The patient made little, if any, improvement, and the chlorpromazine dosage was increased up to 2000 mg. daily. No changes were noted. He was also given a trial on chlorpromazine combined with reserpine and later on azacyclonol, when these drugs were under study, with no response.

He is at present on 150 mg. of chlorpromazine daily. He has remained delusional, autistic, and withdrawn.

He has been rated as having shown no change. He was rated tenth with regard to group adjustment.

Case 11. W. B., a 49 year old man, was first admitted to Topeka State Hospital on May 15, 1931, with a diagnosis of schizophrenic reaction, schizoaffective type. He has been hospitalized on four occasions since that time. He received six electroconvulsive treatments in 1946, with temporary improvement.

In November, 1954, at the beginning of the Feldman study, he was described as resistive, hyperactive, and hostile. It was felt he had good contact with reality, but this was difficult to evaluate since he was withdrawn, mute, and uncooperative. He did not participate in any ward activities, and he avoided any interpersonal relationship. He was placed on 200 mg. of chlorpromazine daily.

In February, 1955, he was rated as having made a marked improvement. He became active in helping on

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the ward and in occupational therapy. He was able to begin an industrial assignment in the kitchen. He stated that he felt like a "different man." He began to make realistic plans for leaving the hospital.

On June 6, 1956, this patient was paroled to a boarding home on a maintenance dose of chlorpromazine (100 mg. daily).

This patient was not included in the present study as he was not available for a clinical evaluation at the time.

SUMMARY

It was the purpose of this study to follow up 10 psychotic patients at Topeka State Hospital, Topeka, Kan., who had been a part of an experimental group in a previous study concerning the effects of chlorpromazine on psychotic behavior. The period of time that had elapsed since the completion of the original study was two and one-half years. A review of the pertinent literature was given with emphasis being placed on follow-up studies of chlorpromazine. The original study was summarized in detail, emphasizing the results found and conclusions reached. The method of assessing change was to compare Fergerson Hospital Adjustment ratings and to compute two clinical rating scales. The conclusions of the investigation were that the patients had made no significant change of adjustment on any part of the Fergerson scale or on the clinical ratings during a period of two and one-half years. However, a closer inspection of the individual patients indicated that some of them had made a striking improvement. The lack of homogeneity of the group studied was felt to influence the negative results. It was felt that the factor of homogeneity might be considered in future research as well as the fact that clinical raters were able to rate patients in a consistent way and that the Fergerson scale and clinical ratings were significantly similar.

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RESUMEN

El propósito de este estudio fue la observación ulterior de 10 pacientes psicóticos del Topeka State Hospital, Topeka, Kansas, que formaban parte de un grupo experimental en un estudio previo relacionado con los efectos de la cloropromazina sobre la conducta de los psicóticos. El tiempo transcurrido desde que se completó el estudio original fue de dos años y medio. En la revisión de la literatura relacionada con el estudio, se hizo hincapié en lo que se refería a la observación ulterior de pacientes tratados con cloropromazina. El trabajo original se resumió detalladamente, destacándose los resultados obtenidos y las conclusiones a que se llegó. El método de valoración de los cambios experimentados por los pacientes consistió en comparar los grados correspondientes de la Escala de Fergerson para valoración en hospitales y computar los grados de dos escalas clínicas. Las conclusiones de la investigación fueron que los pacientes no experimentaron cambios de importancia en su

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adaptación al medio según la Escala de Fergerson o según los grados clínicos, durante un período de dos años y medio. Sin embargo, un cuidadoso examen de cada paciente indicó que algunos de ellos habían experimentado una mejoría notable. La falta de homogeneidad del grupo estudiado parece haber influenciado los resultados negativos. Este factor de homogeneidad se puede considerar en futuros estudios, así como también el hecho de que los evaluadores clínicos pueden evaluar a los pacientes en forma uniforme. Por otra parte, la Escala de Fergerson y las evaluaciones clínicas fueron significativamente similares.

RESUME

Le but de cette étude était de poursuivre l'observation de 10 malades psychotiques au Topeka State Hospital, Topeka, Kansas. Ces sujets faisaient partie d'un groupe expérimental dans une étude antérieure relative aux effets de la chlorpromazine sur le comportement psychotique. La période de temps écoulée depuis la fin de l'étude originale était de deux ans et demi. Une analyse de la littérature pertinente souligne l'intérêt des études comportant la poursuite de l'observation des malades traités par la chlorpromazine. Il a été présenté un compte-rendu détaillé soulignant les résultats observés et les conclusions des investigateurs. La méthode d'évaluation des changements consistait à comparer les "ratings" d'adaptation à l'hôpital de Fergerson et à évaluer deux échelles de "rating" clinique. L'investigation a permis de conclure que les patients n'avaient présenté aucun changement d'adaptation significative en aucun point de l'échelle de Fergerson ou à tout niveau des "ratings" cliniques durant une période de deux ans et demi. Toutefois, un examen plus approfondi de chaque malade révélait une amélioration extraordinaire chez certains d'entre eux. On a supposé que l'absence d'homogénéité du groupe étudié influençait les résultats négatifs et on a estimé qu'il y aurait lieu de tenir compte du facteur d'homogénéité dans les recherches ultérieures, ainsi que du fait que les cliniciens chargés du "rating" avaient les moyens de procéder à l'évaluation des malades d'une manière uniforme et que l'échelle de Fergerson et les "ratings" cliniques étaient notamment semblables.

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Incorporating the International Record of Psychiatry and Neurology

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INCORPORATING INTERNATIONAL RECORD



OF PSYCHIATRY AND NEUROLOGY

FOREWORD

The purpose of the **QUARTERLY REVIEW OF PSYCHIATRY AND NEUROLOGY** is to present promptly brief abstracts, noncritical in character, of the more significant articles in the periodical medical literature of Europe and the Americas.

For ready reference, the abstracts are classified under the following general headings:

PSYCHIATRY

1. Administrative Psychiatry and Legal Aspects of Psychiatry
2. Alcoholism and Drug Addiction
3. Biochemical, Endocrinologic, and Metabolic Aspects
4. Clinical Psychiatry
5. Geriatrics
6. Heredity, Eugenics, and Constitution
7. Industrial Psychiatry
8. Psychiatry of Childhood
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10. Psychiatric Nursing, Social Work, and Mental Hygiene
11. Psychoanalysis
12. Psychologic Methods
13. Psychopathology
14. Treatment
 - a. General Psychiatric Therapy
 - b. Drug Therapies
 - c. Psychotherapy
 - d. The "Shock" Therapies

NEUROLOGY

1. Clinical Neurology
2. Anatomy and Physiology of the Nervous System
3. Cerebrospinal Fluid
4. Convulsive Disorders
5. Degenerative Diseases of the Nervous System
6. Diseases and Injuries of the Spinal Cord and Peripheral Nerves
7. Electroencephalography
8. Head Injuries
9. Infectious and Toxic Diseases of the Nervous System
10. Intracranial Tumors
11. Neuropathology
12. Neuroradiology
13. Syphilis of the Nervous System
14. Treatment
15. Book Reviews
16. Notes and Announcements

In fields which are developing as rapidly as are psychiatry and neurology, it is obviously impossible to abstract *all* the articles published—nor would that be desirable, since some of them are of very limited interest or ephemeral in character. The Editorial Board endeavors to select those which appear to make a substantial contribution to psychiatric and neurologic knowledge and which promise to be of some general interest to the readers of the **REVIEW**. Some articles, highly specialized in character, or concerning a subject already dealt with in an abstract, may be referred to by title only at the end of the respective sections.

A section entitled **INTERNATIONAL RECORD OF PSYCHIATRY AND NEUROLOGY** is included at the beginning of the journal. The Record Section consists of advanced clinical and experimental reports.

The Psychiatry and Neurology Newsletter was compiled by Dr. Peter A. Angelos.

The Editorial Board at all times welcomes the suggestions and criticisms of the readers of the **REVIEW**.

WINFRED OVERHOLSER, M.D.
Editor-in-Chief

QUARTERLY REVIEW OF PSYCHIATRY AND NEUROLOGY

*

ABSTRACTS

psychiatry

ALCOHOLISM AND DRUG ADDICTION

56. *A Comparison of Reserpine and Disulfiram in the Treatment of Alcoholism.* R. E. REINERT, Topeka, Kan. Quart. J. Stud. on Alcohol. 19:617-622, Dec., 1958.

The relative effectiveness of reserpine and disulfiram in helping maintain sobriety was tested in a follow-up study of 48 alcoholics. Half the group was treated with reserpine and half with disulfiram during and after a three month period of hospitalization. Follow-up was supposed to cover a 12 month period; those lost to follow-up were counted as failure. As a whole, the disulfiram group was more accessible to follow-up and had had significantly more months of sobriety than did the reserpine group, even though several patients on disulfiram discontinued the drug. Those patients who suffered most severely from feelings of anxiety, guilt, or rage either did not benefit from or became worse under reserpine treatment. No patient who denied subjective benefit from reserpine had any significant period of sobriety. The hypothesis was advanced that many patients had expected that reserpine would be a substitute for alcohol, and that their disappointment contributed to their early relapses. On the other hand, disulfiram stimulated the better-motivated patients to make the most of their three months of therapy in the hospital.—*Author's abstract.*

57. *The Psychodynamic Functions of Alcohol.* ROBERT I. LEVY, San Francisco, Calif. Quart. J. Stud. on Alcohol. 19:649-659, Dec., 1958.

The drinking of alcohol produces a variety of psychodynamic effects. This article, based on a study made at a specialized clinic for drinking problems, makes a tentative classification of these effects into: (1) Organic effects due to toxic modification of neural functioning, and (2) symbolic effects, or meanings given to the act of drinking, to the perception of the immediate organic effect, to the perception of the long-range toxic effects, and to the perception of the interpersonal effects. The organic effects are divided into discharge and narcotizing aspects. Among the most clinically prevalent symbolic meanings are the evocation of a number of infantile experiences and modes of reaction, a variety of maso-

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chistic meanings, hostile effects, mastery attempts, and attempts at solving identity problems. These effects or functions of the use of alcohol occur in most drinkers; the question arises as to what new element occurs in alcoholism as a chronic pattern. Alcoholism seems to occur in a variety of personality types, especially: (1) If the variety of symbolic and organic effects "solve" a critical number of psychological problems, (2) in certain types of masochistic or infantile personality for which the effects of drinking provide relatively specific gratification, or (3) if the drinking, though initiated for any one of its acute functions, produces a disturbing effect (guilt, anxiety, bodily ill feelings, breakdown of social functioning), and if the effect can only be assuaged, in an individual with a paucity of resources, by further drinking. Illustrative case material is included. 11 references.—*Author's abstract.*

58. *Meprobamate Addiction.* LINN J. BOYD, LEONARD CAMMER, MICHAEL G. MULINOS, VICTOR F. HUPPERT, AND HARVEY HAMMER, New York, N. Y. *J. A. M. A.* 168:1839-1843, Dec. 6, 1958.

The authors designed a clinical investigation method for the purpose of determining the likelihood of addiction to meprobamate. The method included a double control. One group of 60 patients not in need of meprobamate therapy received a 0.4 Gm. capsule of meprobamate three times a day, and a second group of 30 subjects received a placebo. Sudden withdrawal of the meprobamate was made by switching to the placebo, thus obviating disturbances due to the "cessation of medication" syndrome. Despite prolonged use of meprobamate, no evidence of dependence, physical or psychic, was evinced by any of the subjects upon sudden switching to the placebo. In these elderly subjects, about equally divided as to sex, reactions to central depressants would be somewhat exaggerated. However, except for the tranquilizing effects of meprobamate and the increased sleep and diurnal dozing due to it, there was no difference in behavior between subjects taking meprobamate and the controls. The total lack of withdrawal symptoms in these subjects leads the authors to conclude that the occasional occurrence of symptoms reported by others must be ascribable to the ingestion of very large daily doses of meprobamate and to the unbalanced personality that usually leads to such excesses. 5 references.—*Author's abstract.*

CLINICAL PSYCHIATRY

59. *The Meaning of Ethical Concepts for Psychiatry.* HANS HEIMANN, Berne, Switzerland. *Confinia Psychiat.* 1:89-112, Jan., 1958.

Ethical concepts have a normative character, i.e., they establish or help in establishing norms. A threefold significance of ethical concepts in scientific psychiatry is recognized: (1) As regards methodology, these concepts signify a boundary line beyond which psychiatric methods are not applicable. (2) They indicate the anthropological background of psychiatric research where man can be looked at as person in his particular relation to values. (3) In personal existence they may lead to the experience of the irreducible spiritual content of ethical phenomena and thus beyond speculation about apersonal theoretical systems in psychiatry.

As an example of the third aspect there is a consideration of psychoanalysis and of Freud's personality: Freud's personal ethical attitude disagreed and was bound to disagree with his theory on man that he formulated on a natural-scientific basis. The elimination of an apersonal picture of man in psychiatry enables existential analysis to do justice to the ethical sphere without putting the person's relation to values in jeopardy. However, in a personalistic medical anthropology the person's relation to values will take on central significance. This can be demonstrated in the psychiatric attitude toward the freedom of will during the last century and in the modern anthropological tendency of psychiatry. 35 references.—Author's abstract.

60. *The Interpersonal Theory of Psychiatry. The Hypotheses of Harry Stack Sullivan.* LUTZ ROSENKÖTTER, Göppingen, Germany. *Fortschr. d Neurol., Psychiat.* 26:430-440, Aug., 1958.

The wide acceptance of psychoanalytic theories in American clinical psychiatry has been a challenge that has led to a reformulation of certain psychoanalytic concepts. An important contribution in this field has been made by Harry Stack Sullivan. Psychic processes, according to Sullivan, cannot be studied in terms of a "psychic apparatus" but take place and can be observed only in an interpersonal field. The human being has two basic types of need: those determined by his physical organization, such as intake of energy, maintenance of body temperature, and so on, and the need for positive interpersonal relations that offer the individual security and whose absence provokes anxiety. Anxiety or the avoidance of anxiety are the most important factors in the origin of psychic disorders. The individual can experience interpersonal relations in three ways: (1) The prototoxic, mainly undifferentiated bodily sensations during infancy, (2) the parataxic, or individualized, autistic perception that is not shared by others, occurring normally at the beginning of speech development, but in later stages as "parataxic distortions", and (3) the syntactic, where meaning of symbols is shared in "consensual validation." The stages of personality development are described in terms of interpersonal maturation as opposed to libidinal organization (infancy, childhood, juvenile period, preadolescence, early adolescence, late adolescence, maturity). The self is originally the internalized role ascribed to the individual by the significant adults. Anxiety-provoking psychic processes are kept out of awareness by the self, using the dynamisms of sublimation, selective inattention, or dissociation. The application of Sullivan's theories to obsessive-compulsive and schizophrenic disorders of personality is demonstrated.—Author's abstract.

61. *The Changing Conception of Normality and Its Assessment. With Special Reference to Psychiatry.* D. J. SALFIELD, Derby, England. *Acta psychotherap., psychosom., et orthopaed.* 6:144-155, 1958.

Any criterion of cure needs norms of normality, as was discussed in a previous paper. Normality was defined as being "not a state of affairs but homoeostasis in action." The homoeostasis of living matter prevents the dissipation of energy, is the only observable process counteracting entropy, and is similar to or identical with the libido of the various depth psychologies. Homoeostasis or, in different terms, the flow of libido is maintained by

the more than sufficient operation of compensation, i.e., overcompensation. Compensation means the counterbalancing of opposite movements from the center of stability. If we wish practically to manipulate the homoeostasis of man, we have to consider values. We have to reconcile values in the different fields of organic function. There are values which we may properly call anthropological or sociological, statistical, and psychobiological (in terms of a need psychology). If we wish to search for the source of values and the way sets of values are acquired, we have to consider metaphysical systems, especially those that are connected with existentialist views. If we are unable to believe implicitly in revelation and its cousin, intuition, but rather tend to accept psychological observations and inductively obtained conclusions therefrom, we may turn to Jung's *Analytical Psychology* and *Daseinsanalyse* for psychological and systematic attempts at establishing values. Finally, in order to be of practical importance, the idea of homoeostatic efficiency, or, in other words, normality, must be capable of a quantitative determination. This can, on principle, be done by the means of assessment of compensatory effectiveness between the productions of the unconscious, such as dreams, active imagination, automatic drawings, writing induced by hypnosis, and projective techniques and the reality situation. This can be attempted even numerically, e.g., with the author's prognostic scale based on the Rorschach record, described earlier. 11 references.—Author's abstract.

62. *Brain Mechanisms and Psychotherapy*. BERNICE T. EIDUSON, Beverly Hills, Calif. Am. J. Psychiat. 115:203-210, Sept., 1958.

The vigorous experimental work in neurophysiology and neurobiochemistry directs attention toward the structural mechanisms of the central nervous system and particularly to the ways in which and the extent to which these built-in mechanisms order response. The work that has emerged to date has immediate pertinence for some of the problems that have always been crucial ones in personality theory, problems related to the way in which personality is formed, to what personality change is and the way it is brought about, and to the nature and significance of individual differences. As the laws of input organism exchange are extended by subsequent research, and as we begin to think of the therapeutic communication itself as input, we may have to revise sharply our current ways of thinking about the clinical process itself and some of the ideas that are inherent in it. At this point systematic presentations of the clinical and observational data, which are the wealth of the clinical psychiatrist, would be very helpful in establishing the significance of the neurophysiological findings and even in contributing clues as to the directions in which further advance might lie.—37 references.—Author's abstract.

63. *Current Status of the Funkenstein Test. A Review of the Literature Through December, 1957*. IRWIN FEINBERG, Bethesda, Md. A. M. A. Arch. Neurol. & Psychiat. 80:488-501, Oct., 1958.

The literature on the Funkenstein test is reviewed, particularly with respect to the following factors: test procedure and scoring; reproducibility (reliability); relation to psychiatric state, including ability of the test to predict response to psychiatric treatment and to serve as an index of clinical state; and proposed physiological mechanisms. It was

noted that a variety of methods of administration of epinephrine and methacholine and of scoring the blood pressure responses have been employed. These variations may account in part for inconsistencies among results obtained. The reliability of the test appears good under certain conditions of drug administration but poor under others. Available control group data do not adequately match patient populations for age and initial blood pressure level; however, evidence exists that suggests that these are relevant variables that require evaluation. The prognostic value of the test and its ability to mirror changes in the clinical state of the patient cannot yet be regarded as established. For the reasons discussed, it is possible that a correlation between test response and prognosis may reflect only the change in distribution of mental diseases that occurs with advancing age. Various physiological mechanisms have been proposed to explain individual differences in the magnitude of the hypotensive response to methacholine. Such differences have been related to differing levels of circulating epinephrine and arterenol-like substances (Funkenstein) or to differences in hypothalamic excitability (Gellhorn). Neither hypothesis is supported by conclusive evidence. The paper concludes with brief mention of diverse other applications of the Funkenstein test. 58 references. 2 figures. 6 tables.—Author's abstract.

64. *Simple and Choice Reaction Times in Schizophrenia.* ARTHUR L. BENTON, RICHARD C. JENTSCH, AND H. J. WAHLER, Iowa City, Iowa. A. M. A. Arch. Neurol. & Psychiat. 81:373-376, March, 1959.

When the performances of control patients are taken as a standard, schizophrenic patients exhibit a more marked retardation in simple reaction time than in choice reaction time. These findings, which are quite comparable to those previously secured from patients with cerebral disease, indicate that schizophrenic and brain-damaged patients show the same pattern of performance with respect to simple and choice reaction time. Impairment in the performance of simple, high-speed tasks appears to be a salient behavioral feature in many cases of cerebral disease and schizophrenia. This finding can be interpreted in a variety of ways. It might be concluded that those schizophrenic patients who show marked retardation in simple reaction time constitute a special "brain-damaged" subgroup of this category. Alternatively, it might be concluded that, although the underlying pathologic processes are quite different in the two diagnostic categories, a common end result is a motivational or other type of deficit that leads to an over-all retardation in responsiveness. Since consideration of the tenability of these or other hypotheses would require evaluation of a wide range of data, it is beyond the scope of this investigative report. 6 references. 2 figures.—Author's abstract.

65. *Preadaptive Attitudes to Hallucinations in Schizophrenic Patients.* PHILIP P. STECKLER, Syracuse, N. Y. A. M. A. Arch. Neurol. & Psychiat. 80:625-628, Nov., 1958.

This study of a series of patients interviewed at the Syracuse Psychiatric Hospital revealed a consistent pattern of reactions to hallucinations. Initially, the most prominent elements are apprehensiveness and fright. The experience as viewed by the intact portion of the personality is strange, even eerie, causing increased anxiety and fear. The autonomic

system participates in the reaction, as manifested by rapid heart rate, deeper respirations, pallor, sweating, and dryness of the mouth. The skeletal musculature may join in, as evidenced by tremor and tenseness of the muscles. Simultaneously, or in the next stage, the thought of "going crazy" or losing one's mind is experienced. This again evokes marked anxiety. If this reaction is prolonged, depression occurs and may be followed by suicidal thoughts. Some patients adapt to the altered state within a matter of hours, but it may last for days or months. Recollection of this period is present in all the recent cases studied, but the patient most frequently did not present information of the disturbing events spontaneously.

Recognition of this early reaction, especially if the hallucinations remain covert, is important. This period is one of increasing danger to the patient because the fear of insanity produces depression and the possibility of suicide. The therapist can help the patient by expressing his awareness of the patient's plight and fears. It may shorten the illness by preventing the establishment of the common later reactions and by facilitating the reconstitution of the premorbid personality. Certainly an awareness of the initial reaction will promote communication and foster the establishment of a relationship between patient and doctor based on understanding. 4 references.—*Author's abstract.*

PSYCHIATRY OF CHILDHOOD

66. *The Mongoloid and the Problem of His Heredity.* ARTHUR STERN, Jerusalem, Israel. Psychiat. et Neurol. 136:361-370, Dec., 1958.

The author investigated five of his cases of mongolism from the clinical point of view and especially with regard to the occurrence of mongoloid traits in the members of their respective families. Other investigators confirm his observations of frequent occurrence of sub-mongoloid traits ("microsymptoms") in other members of the families of true mongoloids. These observations explain the continued spreading of mongolism and support, furthermore, the investigations of twins (all monozygotes are concordant; most dizygotes are discordant), whereas the occurrence of multiple cases of mongolism in the same family supports the genetic theory of mongolism. A diseased gene is obviously the primary cause. This factor perhaps leads to malformation of the germ plasma (overaging or exhaustion) and consequently to abnormal development of the fetus. Further studies of submongoloid traits in the families of mongoloids will be of great importance in increasing our knowledge in this field. 19 references.—*Author's abstract.*

PSYCHIATRY AND GENERAL MEDICINE

67. *Psychosomatic Aspects of Narcolepsy.* COLIN M. SMITH, Saskatoon, Saskatchewan. J. Ment. Sc. 104:593-607, July, 1958.

The literature relating narcolepsy to emotional disturbance is briefly reviewed. Attention is drawn to the rare occurrence of paranoid psychosis with idiopathic narcolepsy. Two cases of idiopathic narcolepsy are presented. The illness in the first patient was accompanied by paranoid schizophrenia, and in the second by a neurotic character disorder. The relationship between the narcoleptic symptoms and the mental state is discussed.

Rorschach and Minnesota Multiphasic Personality Inventory findings are given. Unusual neurophysiological findings reported included an apparent increase in alertness recorded by the electroencephalograph under insulin-induced hypoglycemia. It was suggested that this alerting effect might be due to a central liberation of adrenaline with stimulation of the adrenaline-sensitive part of the reticular activating system. It is considered that idiopathic narcolepsy is not primarily a psychogenic condition but may be influenced by psychological factors. Both somatic and psychological approaches are indicated in therapy. 72 references. 4 figures.—Author's abstract.

68. *Psychosomatic Aspects of the Common Cold. A Preliminary Report.* DANIEL CAPON, Toronto, Ontario. *Canad. M. A. J.* 79:173-180, Aug. 1, 1958.

Some 400 patients were surveyed in a preliminary study to attempt to uncover the nature of associations, if any, between the common cold and the person, that is, the possible psychosomatic aspects of the common cold. The experimental group of psychiatric patients had two and one-half times more frequency and duration of "colds" compared with the control group of nonpsychiatric patients. The successfully treated psychiatric patients approximated to the controls as regards "cold" frequency and reaction (at the 0.01 level of confidence on mean test). Repeated clinical observations were made on the alleviation or abolition of nasal allergies, postnasal dripping, and "colds" during treatment hours and after the course of treatment. A "cold" index can be fashioned into a measure of successful psychotherapy. Mucosal turgescence probably mediates the psychological correlate of "resistance" to infection.

There were three clinical groups, illustrated with case reports: In the first, psychogenic factors favor colds but the psychopathology is not specific. In the next, psychogenic factors seem to predispose specifically to upper respiratory infections. In the last, psychogenic factors seem to actually oppose (or ignore) colds.

The author suggests that, from the point of view of mental hygiene, colds may provide an innocuous emotional substitute and outlet, and a legitimate excuse for regression, rest, and recovery that, if physically denied, may result in worse psychic or psychosomatic damage. 18 references.—Author's abstract.

69. *Medical, Psychiatric, and Legal Aspects of Premenstrual Tension.* IRWIN N. PERR, Cleveland, Ohio. *Am. J. Psychiat.* 115:211-219, Sept., 1958.

Premenstrual tension is characterized by headache, nausea, lethargy, dizziness, depression, irritability, edema, mastalgia, tension, emotional lability, anxiety, insomnia, and thirst in the week prior to menses. Symptoms occur in various combinations and to various degrees in from 30 to 95 per cent of women. Theories regarding cause fit into various categories. Water retention due to hormonal and electrolyte imbalance is responsible for many of the physiologic symptoms. The psychologic symptoms do not relate well with the physiologic symptoms, so that diuresis is not directly related to emotional symptoms. Basically, water retention is related to a change in the estrogen-progesterone ratio. Reports disagree on such physiologic findings as basal temperatures, endometrial biopsies, and urinary hormonal assays that measure primarily the presence or absence of anovulatory

menstruation. Another common finding is a "relative" or "subclinical" hypoglycemia that is not marked enough to merit a diagnosis of hypoglycemia. Glucose tolerance curves similar to other disturbances involving stress are found.

The syndrome is based on a physiologic stress of a mild degree occurring within relatively narrow limits. The emotional reactions to the stress depend on the personality and not the stress. It seems doubtful that there is a premenstrual psychosis unassociated with other findings. Usually a basically psychotic personality is found in cases where premenstrual symptoms reach a psychotic degree, and the classification of premenstrual psychosis as a unique category is unjustified. The emotional symptoms are not well related to physiologic symptoms but reflect the individual's characterologic make-up. Although some have attempted to equate premenstrual tension, with or without hypoglycemia, to temporary insanity, such a correlation appears unjustified. One writer even suggested that this "insanity" could be verified by a vaginal smear. However, laboratory tests are of little value. Diagnosis depends on history and over-all medical evaluation; diagnosis alone is meaningless, since most women can be so diagnosed. Hypoglycemia severe enough to cause "psychosis" should be evaluated alone and not as a part of the syndrome. A single episode of "temporary insanity" is most unlikely. There should be corroboration of psychosis from history and medical evaluation both before and after an alleged psychotic episode. It is possible that consideration of the premenstrual tension syndrome may be helpful in clarifying certain legal situations. Treatment often helps the emotional symptoms and may lessen acting-out with its accompanying adverse social consequences. 47 references.—Author's abstract.

70. *Comments and Observations on Psychogenic Hypersomnia.* COLIN M. SMITH, Saskatoon, Saskatchewan. A. M. A. Arch. Neurol. & Psychiat. 80:619-624, Nov., 1958.

The literature on psychogenic hypersomnia is briefly reviewed. It is pointed out that patients appear to fall into two groups: (1) Patients who suffer prolonged pseudosleeps that may last for weeks or months. Clinically and electroencephalographically these are not true sleep attacks, although genuine sleep may appear intermittently. (2) Those who are subject to oversleeping that rarely lasts longer than 24 hours and is probably a true sleep. Both types of case are to be distinguished from the narcolepsy-cataplexy syndrome. A case is presented of a 56 year old man who suffered from prolonged attacks of what had been regarded as "sleep." On one occasion he had "slept" for 52 days. There was a clear relationship between these attacks and repressed hostility. Clinically his condition during an attack was quite distinct from normal sleep. The electroencephalogram showed a waking pattern with only occasional drowsiness. Projective tests indicated that he had a great fear of his affective life because of underlying hostility and confusion regarding his sexual identification. 42 references. 2 figures.—Author's abstract.

71. *A Project for the Creation of Better Understanding of Psychiatry by the General Practitioner.* CHARLES E. GOSHEN, Washington, D. C. South. M. J. 52:30-34, Jan., 1959.

Since 1957, the American Psychiatric Association has been developing a program designed to create interest in and facilities for the psychiatric training of family physicians. These

efforts are in recognition of the generally inadequate undergraduate training in basic psychiatry in the past. The area of preventive mental hygiene is the one in which the family physician (and pediatrician) will find an increasingly important role. Psychiatric practice is geared today to the care of patients who are quite well along in the development of their psychiatric problems, and it seems unlikely that psychiatrists themselves will be numerous enough to tackle the nation's number one public health problem at the preventive level. Not only is the family physician in a position to do something to prevent the tragedy of hospitalization for mental disease, but he could also do a great deal to prevent juvenile delinquency, alcoholism, divorce, and other forms of social disability. The family physician is already armed with an interest in human welfare at an individualized level and a long medical tradition of a sense of responsibility for the total patient. What he generally lacks, however, is the basic skills of everyday psychotherapy. With specific training at a post-graduate level, he can develop sufficient skill to make proper diagnosis and referral and to handle the actual treatment of many of the minor problems. Probably 30 per cent of his patients could benefit from this skill.—*Author's abstract.*

PSYCHIATRIC NURSING, SOCIAL WORK, AND MENTAL HYGIENE

72. *Drop-out from Outpatient Psychiatric Treatment. "Personality" and Situational Determinants.* NORBERT FREEDMAN, DAVID M. ENGELHARDT, LEON D. HANKOFF, BURTON S. GLICK, HARVEY KAYE, JULIUS BUCHWALD, AND PAUL STARK, Brooklyn, N. Y. A. M. A. Arch. Neurol. & Psychiat. 80:657-666, Nov., 1958.

Fifty-four ambulatory schizophrenic patients attending an outpatient clinic were divided into those who voluntarily dropped out of treatment after eight sessions or less (25) and those who remained active for nine sessions or more (29). The groups were found to be matched for age, sex, referral source, and a number of psychopathologic characteristics. An attempt was made to differentiate the two groups on the basis of information available from the first clinic contact. The personality characteristics of the patient were rated at the time of intake by the clinic psychiatrist. A relationship index based on a content analysis of the doctor's notes of the initial contact was developed, which provided us with an objective measure of "warmth" or "detachment" of relationship. In our sample, drop-out patients were rated as slightly higher on "adaptive" traits than were active patients ($P < 0.06$). When the extremes of drop-out patients (three weeks' clinic attendance or less) were compared with the extremes among active patients (eight months' attendance or more), the differentiation was more significant ($P < 0.02$). However, this increased differentiation could not be attributed to a higher "adaptation" score for the extremes among drop-out patients but, rather, was attributed to a lower score for the extremes among active patients. Drop-out patients did not differ from active patients in terms of the "warmth" of the doctor-patient relationship encountered during the initial contact. However, when the relationship was matched with the patient's expectation about treatment, a significant interaction emerged. Patients denying mental illness and encountering a "warm" relationship tended to drop out; patients accepting their own illness and encountering a "warm" relationship tended to remain in treatment. On the basis of these

observations, we tested the more general hypothesis that a doctor-patient relationship consistent with a patient's expectation about treatment would facilitate continuation in treatment and that an inconsistent relationship would facilitate drop-out. The hypothesis was confirmed for 30 of the 41 patients who were studied, that is, significant beyond the 0.01 level of confidence. 12 references. 3 tables.—Author's abstract.

TREATMENT

a. General Psychiatric Therapy

73. *Recent Advances in the Treatment of Schizophrenia: Group Training and the Tranquillizers.* DONALD BLAIR AND DESMOND M. BRADY, Southall, England. *J. Ment. Sc.* 104:625-664, July, 1958.

This article describes the results of seven years of clinical research on schizophrenia. The authors first discuss the effects achieved from four years of group training of chronic schizophrenic patients. By the end of this period, the maximum effects that could be expected from group training had been achieved and an excellent control situation for observing the effects of the ataraxics was presented. Using the same patients, the effects of reserpine and chlorpromazine were compared over a period of six months. Chlorpromazine was so much more effective that subsequent work was confined to it. After experience with 132 chronic schizophrenic patients, the authors evolved a technique for the optimum effect of chlorpromazine, which entailed in most cases the concomitant use of Artane (found to be synergistic), thyroid, and courses of electroconvulsive therapy. This technique is described in detail; because of the clinical results obtained, the authors feel that the maximum results from chlorpromazine will only be derived by being fully cognizant of its properties and by using the technique described or a similar one. The technique was next applied to 124 recent cases of schizophrenia, and again the therapeutic results were outstanding. Patients were classified in the following categories: Recovery, social recovery, much improved, improved, and worse. A comparison was made of the effects of chlorpromazine and insulin coma therapy over the previous five years, showing much better results from the former. 72 references. 42 figures. 6 tables.—Author's abstract.

74. *Psychiatric Occupational Therapy: Some Aspects of Roles and Functions.* MADELAINE ELLIS, OTR BACHRACH, AND ARTHUR J. BACHRACH, Charlottesville, Va. *Am. J. Psychiat.* 115:318-322, Oct., 1958.

The occupational therapy situation as a permissive one allows for diagnostic evaluation that can parallel other diagnostic approaches. Occupational therapy provides an opportunity for a flexible situation in which the patient himself selects the tasks in contrast to the psychological examination in which the tasks or problems are necessarily standardized and selected by the psychologist. A coupling of both approaches appears fruitful. The problem-solving aspects of occupational therapy offer an opportunity to evaluate such critical behavioral factors as the manner in which the patient approaches a task, the type of task he selects, the nature and degree of help he solicits, and his movements toward completion, as well as the level and character of group interaction. By keeping the occu-

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pational therapy situation flexible, its diagnostic and therapeutic values are enhanced. The major part of this brief exposition of behavioral aspects of occupational therapy is devoted to an analysis of the characteristics of occupational therapy developed within a framework provided by Waring for child guidance. The authors have adapted and reworked this as a model for occupational therapy; it consists of four key principles under which patient-therapist interaction may be conceived. These are: (1) Affection, which tends to develop a sense of value as a person, (2) respect, which tends to develop confidence in one's ability to do, (3) help, which tends to develop assurance that others will supplement the individual's effort as needed, and finally (4) approval, which tends to develop encouragement and direction in the individual's effort, and recognition of his achievement. These four principles allow the person approaching occupational therapy to develop a rudimentary conceptual model. 4 references.—*Author's abstract.*

b. Drug Therapies

75. *Effects of Lysergic Acid Diethylamide (LSD-25) on Intellectual Functions.* ARTHUR B. SILVERSTEIN AND GERALD D. KLEE, Baltimore, Md. A. M. A. Arch. Neurol. & Psychiat. 80:477-480, Oct., 1958.

The purpose of this investigation was twofold: (1) To determine whether memory for various kinds of material is differentially affected by lysergic acid diethylamide (LSD-25), and (2) to check rigorously the clinical impression that this drug impairs the ability to interpret proverbs, a common test of abstract thinking. The Wechsler Memory Scale and the Gorham Proverbs Test were administered to 16 young male college graduates under control conditions, and also after they had ingested 72 µg. of LSD-25 in distilled water. The interval between test sessions was two days. The drug significantly impaired memory only for certain kinds of material. The ability to draw geometric figures from memory, to reproduce brief prose passages, to count backward, say the alphabet, and perform serial addition were all affected. On the other hand, the ability to learn paired associates and to repeat series of digits, orientation for time and place, and memory for personal and current information appeared to be unaffected at the dose level employed. LSD-25 also significantly impaired abstract thinking, as measured by the ability to interpret proverbs. The difference between scores under control and drug conditions resembled the difference reported between the scores of normal subjects and chronic schizophrenic patients. Contrary to expectations, incorrect abstractions proved to be more numerous than concrete responses not only under control conditions but also in the drug state. 13 references. 2 tables.—*Author's abstract.*

76. *Use of Perphenazine in 100 Hospitalized Patients.* HARRY F. DARLING, Hathorne, Mass. Dis. Nerv. System 19:428-429, Oct., 1958.

Perphenazine, a phenothiazine derivative, was given to 100 hospitalized patients, 75 per cent of whom were chronically disturbed. Average starting dose was 43 mg. daily; average maintenance dose was 29 mg. Seventy-one per cent of the patients were schizophrenic and 16 per cent were psychotic mental deficient. Of the 75 chronic patients, the

drug was discontinued in 50, mostly because of parkinsonism (21) or minimal or less than minimal improvement (23). The drug was quite effective on the newly admitted patients. Of the total 100 patients, 41 showed parkinsonism to some degree; the more severe effects occurred on a dose of 48 mg. or more. Leukopenia was not observed. Two patients had grand mal type seizures. Incidence of akathisia and depression were low. The drug was particularly advantageous in that it did not produce great flattening of affect, and not particularly advantageous where high doses were necessary to produce great flattening of affect. 5 references.—Author's abstract.

77. *Applicability of Sustained-Release Psychopharmacologic Agents to Psychiatric Treatment.* MARKS G. JACOBY, OSCAR PELZMAN, AND H. BABIKIAN, Central Islip, N. Y. Dis. Nerv. System 19:431-434, Oct., 1958.

Chlorpromazine and prochlorperazine have recently become available in sustained release form. This is prepared as hundreds of minute pellets that are either uncoated or are coated with varying thicknesses of a digestible material. After ingestion, there is an immediate release of medication followed by further release of small amounts, thereby extending the psychopharmacologic effects for 12 hours. Chlorpromazine and prochlorperazine in sustained release form were administered to 80 psychiatric patients for periods up to one year; 52 patients were hospitalized psychotics and the remainder were private, nonhospitalized patients with a variety of psychiatric conditions. Total daily dosage of chlorpromazine ranged from 150 mg. to 1200 mg., and daily dosage of prochlorperazine was approximately one third or one quarter that of chlorpromazine. Doses were administered once or twice a day. It was found that giving the drugs in sustained release form once or twice a day: (1) Supplanted the administration of equivalent doses of the drugs on a more frequent schedule; (2) produced a beneficial psychological effect on some patients; (3) reduced the incidence of certain side effects, such as taking naps until the peak effect of the dose had passed; (4) permitted a greater latitude of safety in nonhospitalized patients; and (5) reduced the work load of nursing personnel, permitting them to spend more time with the patients in other rehabilitative therapies. 4 references. 1 table.—Author's abstract.

78. *The Effect of Reserpine on the Duration of Manic Attacks.* DAVID C. WATT, Bucks, England. J. Neurol., Neurosurg. & Psychiat. 21:297-300, Nov., 1958.

Two groups of manic attacks occurring in female patients are compared. Group 1 consisted of 19 attacks, at an average age of 43.7 years, range 17 to 68 years (standard deviation was 11.5). These were all the women admitted to St. John's Hospital, Stone, from December, 1955, to February, 1957. The only specific treatment given to this group was reserpine, 8 to 15 mg. daily for 2 to 10 weeks. Group 2 comprised 44 attacks of mania in 32 patients, at an average age of 46.6 years, range 20 to 72 years (standard deviation was 16.1). These were all women discharged from the same hospital during 1951 to 1955. Treatment was by various methods; the majority had had no specific treatment. Diagnosis was made by the author according to standard textbook descriptions, in some cases confirmed by previous or subsequent attacks of affective illness. It was found that for group 1 the average duration of hospital stay was 11.0 weeks (range 3 to 22, standard deviation

11.3), and for group 2 19.0 weeks (range 3 to 50, standard deviation 11.4), this difference being significant ($t = 2.90$, $p < 0.01$, d.f. = 61). No material differences were found between the two groups for the average length of the period (1) between onset and admission and (2) between recovery and discharge. Eight patients had had several attacks of mania, one of which, in each patient, was treated with reserpine. The average duration of the reserpine-treated attacks was 13 weeks less than the average duration of attacks not so treated. Group 2 was split, and it was shown that there was no difference in average duration of hospital stay between those attacks occurring in the period 1951 to 1952 and those in 1953 to 1955. The difference in average duration of hospital stay between groups 1 and 2 is unlikely, therefore, to have been caused by a change in hospital policy. It cannot be explained by earlier discharge following recovery in the reserpine-treated group, and it is concluded, therefore, that reserpine does shorten manic attacks. 37 references. 1 figure. 2 tables.—Author's abstract.

79. *Effects of Two Phenothiazine Drugs on Concentrative Attention Span of Chronic Schizophrenics.* PAUL G. DASTON, Brockton, Mass. *J. Clin. Psychol.* 15:106-109, Jan., 1959.

Twenty-six chronic schizophrenic patients, subjects in a double-blind study of chlorpromazine, promazine, phenobarbital, and placebo effects on gross behavior, were tested for changes in concentrative attention span. This function, notably impaired in chronic schizophrenia, is associated with impaired learning ability and memory for meaningful materials. Two Wechsler Memory Scale subtests, which assess learning ability and immediate memory, were employed to evaluate the effects of these drugs. There were statistically significant differences favoring both phenothiazine drug groups as opposed to other groups in paired associative learning. On immediate memory, trends favored both phenothiazine drug groups. The paired associative materials were repetitive in nature, whereas the immediate memory materials were presented only once. This may have accounted for the fact that, even though performance on both tasks favored phenothiazine drug groups, paired associative learning was relatively more enhanced. It was concluded that small increments in span of concentrative attention may have been associated with these increases. 10 references. 2 tables.—Author's abstract.

80. *Comparison of Two Phenothiazine Derivatives and a Barbiturate in Chronic Schizophrenia.* JACKSON A. SMITH, CARL GOULDMAN, AVONELL RUTHERFORD, AND JACK WOLFORD, Omaha, Neb. *A. M. A. Arch. Neurol. & Psychiat.* 81:97-99, Jan., 1959.

A group of 75 chronic schizophrenic patients were given chlorpromazine, promazine, mephobarbital, and a placebo as a double-blind procedure; 62 of the patients completed the study. Each patient was given all four medications, with a 7 to 10 day interval between trials. Eighteen patients showed some degree of improvement, but in only 7 was this improvement considered marked. None of the patients was sufficiently improved to be considered for discharge. On the basis of the results obtained, none of the three preparations appears to be the answer to the problem of the chronic schizophrenic patient hospitalized two years or longer. Mephobarbital was as effective as chlorpromazine in producing marked improvement in these patients and more effective than promazine. Neither the history

nor the behavior of the 18 patients who improved was sufficiently unique to permit one to predict, prior to treatment, which patients would be more likely to respond. 3 references.—*Author's abstract.*

81. *Studies on Lysergic Acid Diethylamide (LSD-25). III. Attempts to Attenuate the LSD-Reaction in Man by Pretreatment with Neurohumoral Blocking Agents.* HARRIS ISBELL, C. R. LOGAN, AND E. J. MINER, Lexington, Ky. A. M. A. Arch. Neurol. & Psychiat. 81:20-27, Jan., 1959.

The induction of a psychosis by lysergic acid diethylamide (LSD-25) has been ascribed by various authors to either an excess or a deficiency of the "neurohumors," serotonin, epinephrine (or norepinephrine), and acetylcholine. An effort was made to test these hypotheses by giving the serotonin blocker, 1-benzyl-2-methyl-5-methoxytryptamine (BAS), the adrenergic blocker, phenoxybenzamine, and the acetylcholine blocker, scopolamine, prior to administration of LSD. It was hypothesized that, if the LSD psychosis was due to a relative deficiency of any of the neurohumors, administration of the appropriate blocker would enhance the psychosis. If, on the other hand, it was due to an excess of neurohumoral effect, administration of a blocker should attenuate the psychosis. A crossover experimental method was utilized in which 10 to 12 patients received, on different occasions, LSD alone, LSD plus the blocker, the blocker alone, and a placebo under double-blind conditions. Measurements included change in the size of pupils, blood pressure, and patellar reflex, and degree of mental effect as judged by a questionnaire and a grading system. No significant attenuation of LSD psychosis was observed after any of the treatments. 38 references. 3 tables.—*Author's abstract.*

e. Psychotherapy

82. *A Clinical Evaluation of the Method of Direct Analysis in the Treatment of Psychosis.* KATHERN M. MC KINNON, New York, N. Y. J. Clin. Psychol. 15:80-96, Jan., 1959.

The purposes of this paper are: (1) To present the author's formulations regarding the psychologic rationale underlying Rosen's method of direct analysis in the treatment of psychosis, (2) to suggest the extent to which the personality of the therapist may be a determining factor in the therapeutic process, and (3) to indicate basic similarities and differences between direct analysis in the treatment of psychosis and psychoanalysis in the treatment of neurosis. One of the unique features of Rosen's treatment is the rapidity with which he establishes communication with psychotic patients, arouses their awareness of him, an object in the outer world, and thus causes an interference with their autistic preoccupations within a relatively brief period of time. This achievement requires from the therapist knowledge and resourcefulness essential for understanding, interpreting, and communicating with a psychotic patient in the language of the primitive symbolic imagery of the unconscious, and the capacity and stamina for a strong emotional involvement to the extent that the patient is as important to the therapist as his own child or a member of his family. It is the author's premise that the resolution of psychic conflicts in psychosis by the method of direct analysis occurs through the process of working with the patient's

transference symptoms and resistances, as in psychoanalysis. However, because of the psychotic condition, the therapist's methods must be concrete, vivid, imaginative, and immediate to correspond with the hallucinatory thinking of the patient while he is under the unconscious level of his personality. When the patient's ego capacities become available to him, he may then become accessible to the more traditional psychoanalytic procedures. Principles underlying treatment by direct analysis, as well as methods used by Rosen in handling the transference and resistances with a variety of patients who show negligible or only fragmentary conscious ego functioning, are described and documented with abundant clinical material from treatment sessions observed by the author. The last section of the paper contains a condensation of consecutive treatment sessions over a period of two months in the case of 1 patient who progressed from a deeply psychotic condition to a state of reliable and securely established contact with reality. 12 references.—*Author's abstract.*

d. The "Shock" Therapies

33. *Fear and Anxiety Concerning Electric Shock Therapy.* ALFRED GALLINEK, New York, N. Y. *Confinia Psychiat.* 1:51-56, Jan., 1958.

Of 100 patients treated with electroshock, 67 had marked, but various, degrees and modalities of fear. No relationship could be established between existence or absence of fear and results of therapy. In the majority of patients, no relationship could be established between diagnostic classification on one side and fear of the treatment on the other. Reasonable concern and apprehension that could be dispelled by information and reassurance were not considered to fall under the concept of fear and anxiety. The following categories of fear were observed:

1. Somatogenic fear induced by inconsequential physical sequelae of the treatment, such as postanesthesia hangover, headaches, nausea, memory impairment, and muscle ache.
2. Unreasonable concern and fear in premorbidly anxious patients: Manifestations and conscious motivations of this type of fear do not qualitatively differ from what may be considered as reasonable concern. However, the degree is much higher and the fear can not be dispelled or corrected. These patients are premorbidly anxious people with pre-existing neurotic difficulties. Their fear is attached to the concepts of electricity shock and loss of consciousness. This type of fear tends to diminish with the progress of the treatment.
3. Fear of the treatment as part of the structure of the psychosis: Paranoid and depressive patients occasionally may consider treatment as a hostile persecutory act or as a deserved punishment. This type of fear is rare.
4. The frightening experience of unfamiliarity, disconnection from past and future: This type of fear is most frequent and most disturbing. In contradistinction to the patient who wakes up from general surgical anesthesia, the patient treated with electroshock recovers memory and orientation considerably later than he recovers consciousness. Waking up after shock therapy he finds himself disconnected from his past and also unable to project himself into the future. His inability to recover recent and even remote mnemonic material becomes more pronounced with the progress of treatment. The repetitive administration of electroshock results in a progressive disconnection from past and future that causes

strong affective repercussions. The disconnection from past and future is associated with an experience of unfamiliarity. It is like being in another world. It is only after one hour that things and faces look familiar again.

The hypothesis may be offered that the basic anxiety characterizing man's being in the world is normally neutralized by his sense of familiarity. The familiarity of environment, of life in general, of ourselves, is reassuring. Under normal conditions we know our place in time. Our recollection of and relation to the past is as established as our ability to project ourselves into the future. All these familiar aspects may be obscured during the awakening after electroshock. A temporary annihilation of the sense of familiarity after electroshock provokes basic anxiety and results in a strong, progressively increasing fear of the treatment. 14 references.—Author's abstract.

neurology

CLINICAL NEUROLOGY

84. *The Use of Pneumoencephalography in the Diagnosis of Headache and Epilepsy.* M. GUEST AND D. P. JONES, Vancouver, British Columbia. *Canad. M. A. J.* 79:170-172, Aug. 1, 1958.

The case records of 514 consecutive patients subjected to air encephalography at the Vancouver General Hospital from January, 1955, to June, 1957, were reviewed. Of these, there were 175 patients whose only presenting symptoms were headache and/or epilepsy. These patients were divided into two groups: those without and those with recorded abnormality in physical signs, cerebrospinal fluid pressure and protein, or skull roentgenograms. There were 114 patients in the group without normality, only one (or less than 1 per cent) of whom was found to have a mass lesion, and this patient should possibly have been in the second group, since examination of the cerebrospinal fluid had been omitted and at the time of the pneumoencephalogram it was thought to be under increased pressure. Of the second group, 16 (or 26 per cent) were found to have mass lesions. It is felt that pneumoencephalography is of little practical value in detecting a mass lesion in the diagnosis of headache and epilepsy in patients who, after a thorough examination, have no abnormality in physical signs, cerebrospinal fluid, or skull roentgenogram. In these cases, since the examination is not without risk and morbidity, the disadvantages outweigh the benefits. 5 references. 2 tables.—Author's abstract.

85. *Plasticity of the Human Abdominal Skin Reflex.* K. E. HAGBARTH AND E. KUGELBERG, Stockholm, Sweden. *Brain* 81:305-318, Sept., 1958.

As demonstrated in an earlier electromyographic study, the human abdominal skin reflex has the characteristics of a protective withdrawal reaction, and its latency is short enough

to prove that it is mediated by a spinal reflex arc. In the present study it is shown that the reflex also has plastic properties that cannot be accounted for by spinal function alone. The strength of the motor response and the amount of motor radiation (to distant muscle groups) depends to a large extent upon the subject's "state of expectancy" in regard to the intensity of the abdominal skin stimulus. Reflexes to skin stimuli of low intensity could be exaggerated into forceful withdrawal reactions (involving also the muscles of the extremities) simply by a preceding false statement that the stimulus intensity should be raised, and the reflexes usually diminished when the subject was convinced that no painful stimuli would occur. The reflexes were regularly weak in response to autostimulation. Repetition of a nonpainful stimulus regularly caused a decline and often an enduring total extinction of the reflex response (habituation) even though the motor units involved in this response reacted as promptly as before to other kinds of peripheral stimuli. Furthermore, a single intervening abdominal pain stimulus was often sufficient to cause a lasting sensitization to succeeding weak stimuli within the same skin area. The effects of habituation and sensitization often persisted for several hours. It is concluded that the adaptability of the reflex is due to cerebral governing of the excitability of those spinal interneurones that mediate the reflex. The results are discussed in relation to the theories of conditioning and their clinical relevance is evaluated. 46 references. 5 figures.—Author's abstract.

86. *The Biochemistry of Neuroallergic Reactions.* I. HUSZAK, Szeged, Hungary. Psychiat. et Neurol. 136:215-235, Oct.-Nov., 1958.

In the pathomorphological picture of the neuroallergic reactions in those cases in which the necrosis of the tissue also take place, the most striking feature is the destruction of the myelin sheaths, the so-called demyelination process. To recognize the pathochemical process leading to demyelination, knowledge of the intact biological and biochemical conditions is indispensable. In discussion of the biochemical and biological relations of the nervous tissue it was revealed that, if any member of the complex enzyme of the oxidoreduction systems maintaining the intact structure of the myelin sheaths is inhibited or gets damaged, destruction of the myelin sheath may ensue. The constitutional chemical structure and metabolism of the white matter is more sensitive and less capable of restitution than the gray one. However, in the study of neuroallergic tissue damage one cannot simply stop with the analysis of tissue reactions. It would also be wrong to say that the complex biochemical processes leading to demyelination are due to one factor only; it is necessary to consider a group of factors in which single factors can be classified according to whether their point of attack is direct or indirect. In pathologic reactions leading to tissue necrosis, in addition to the local factors the pathologic functions and metabolic changes of the whole organism play a certain role too. With regard to the factor directly involved in bringing about the lesion of the nervous tissue, there can be little doubt that the antigen-antibody reaction taking place in the parenchyma is essentially the factor directly exerting its effect on the metabolism of the nervous tissue. The biochemical path of the molecular chain reactions leading from the linkage of the antigen-antibody reactions to the demyelination is still unknown. For a working hypothesis, the following suggestions may be taken into account: (1) The products of the enzymatic tissue reactions induced

by an antigen produce substances that inhibit the enzyme system that maintains the structure of myelin sheaths. (2) The adaptive enzyme specific to the antigen can exert damaging effect on the different constituents of the myelin sheath. (3) On the other hand, in the course of the antigen-antibody reaction very potent biological substances are released and accumulated (biogene amine) that may also cause functional disturbances of the enzyme system that plays a role in the maintenance of the myelin structure. The role of biogen amines in the neuroallergic tissue reactions was discussed. In allergic reactions the pathologic changes of vascular system are dominating phenomena. Besides the changes of permeability of the vessel walls, the slowing and the stasis of circulation or venous thrombosis are agents causing tissue lesions. 47 references.—Author's abstract.

87. *Hidden Neurologic Mechanisms in Motor Function Restitution. Experiments with Cortical Lesions in Monkeys.* A. M. LASSEK AND SARA L. EMERY, Boston, Mass. *Neurology* 9:107-110, Feb., 1959.

Intraperitoneal injections of phenobarbital sodium in certain nonlethal dosages produce a state of motor prostration in monkeys showing restitution of motor function after superficial, bilateral lesions of area 4. The duration of this deficit is from 2 to 10 times longer than the period of hypnosis produced. This general result has been obtained repeatedly after spaced injections extending over an interval of 30 months in 1 animal. In 1 case, a monkey has been kept in a continuous state of motor paralysis for as long as a month by giving daily graded doses of the barbiturate. It is suggested that the underlying neurologic mechanisms remaining after the lesions are made are unaffected throughout and are masked by the phenomenon of restitution of motor function. Phenobarbital sodium is a relatively powerful drug that, when injected intraperitoneally into the monkey, reveals latent motor deficits more easily than amobarbital sodium. It is believed that phenobarbital sodium may also prove more efficient in this respect than amobarbital sodium in man. 15 references.—Author's abstract.

CONVULSIVE DISORDERS

88. *Clinical and Electroencephalographic Observations in Alzheimer's Disease.* F. LETEMENDIA AND G. PAMPIGLIONE, London, England. *J. Neurol., Neurosurg. & Psychiat.* 21:167-172, Aug., 1958.

This paper describes the electroencephalographic findings in 17 cases of Alzheimer's disease. All cases were verified histologically, 12 from necropsy material and 5 from cerebral biopsy. The findings were absent or scanty alpha rhythms; generalized 2 to 7 cycles/second activity poorly affected by sensory stimuli, slightly increased by overbreathing but clearly diminished during drowsiness; well-preserved responses to photic stimulation; and poor fast activity response to barbiturates. In induced barbiturate sleep, sleep spindles were recognizable though often of low amplitude; K complexes were only infrequently evoked by sensory stimuli. The EEG abnormalities were fairly uniform in all cases, and there was no constant relationship to the duration and severity of the clinical picture, the presence or absence of fits, or the patient's age. The authors conclude that careful EEG

investigations may help the clinician in the differential diagnosis of patients presenting with dementia in the presenium. 17 references. 4 figures. 1 table.—*Author's abstract.*

89. *A New Drug for Petit Mal Epilepsy.* FREDERIC T. ZIMMERMAN AND BESSIE B. BURGEMEISTER, New York, N. Y. *Neurology* 8:769-775, Oct., 1958.

This article reports upon the effect of PM 671 in controlling or reducing petit mal attacks in 109 patients, many of whom were considered intractable cases. PM 671, on the basis of effectiveness against petit mal attacks, mildness of side effects, and holding ability, offers more promise than other succinimide compounds and medications tested in the past 10 years. Quick and dramatic reduction of attacks occurred in most of 109 patients studied, and side effects were mild and infrequent. Side reactions were occasional drowsiness and dizziness, with some nausea and gastric distress, usually on high doses. Nausea and gastric distress are basic side effects to all succinimide compounds, but fortunately they are rare and not particularly disturbing. No deleterious changes in the blood picture have been noted to date, and urinary findings are within normal limits. No skin rashes have been noted. Studies revealed that PM 671 is also outstanding in the lack of "slippage," or the property in a drug of slowly losing its holding power. Quite a few patients never before helped by any drug have been completely controlled for several years on PM 671. For the group as a whole, an over-all 85 per cent reduction in attacks was obtained in the treatment of petit mal epilepsy. Complete control of petit mal attacks was secured in 42 per cent of patients treated, practical control with an 80 to 99 per cent reduction in attacks in 24 per cent, and partial control with a 5 to 79 per cent reduction in 26 per cent. Experience to date indicates that PM 671 is essentially a petit mal drug. It appeared to be much more effective in the treatment of pure petit mal cases (where pure petit mal existed alone or was combined with other types of seizures) than when a "mixed" petit mal element was present. Results showed that 83 per cent of all pure petit mal cases had a reduction in attacks of at least 80 per cent after therapy; only 29.5 per cent of the mixed petit mal cases reached this high level of control. The individual frequency of attacks likewise did not appear to have any relation to the effectiveness of medication. 3 references. 2 figures. 6 tables.—*Author's abstract.*

DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

90. *Cerebellar Hypoplasia Associated with Systemic Degeneration in Early Life.* R. M. NORMAN AND H. URICH, Bristol, England. *J. Neurol., Neurosurg. & Psychiat.* 21:159-166, Aug., 1958.

Cerebellar hypoplasia has been found to be associated with neuronal degenerative lesions of a systemic character in 2 young infants. The first case was one of pontoneocerebellar hypoplasia and showed, in addition to the usual developmental anomalies of the griseum pontis, arcuate nuclei, and inferior olives, the involvement of other brain stem nuclei including the perihypoglossal and certain midline groups in the medulla. This distribution of lesions was remarkably similar in detail to that previously reported in olivopontocerebellar atrophy. Severe degeneration was present in the dentate nuclei, and transneuronal atrophy

had occurred in the ventrolateral nuclei of the thalamus. Another instance of chain degeneration was seen in the combined atrophy of the mammillary bodies and the anteroventral thalamic nuclei. In the second case, cerebellar hypoplasia was accompanied by absence of the corpus callosum and pyramidal tracts. The dentate nuclei showed a combination of mild developmental arrest and atrophy. Severe and recent degeneration was present in the corpora Luysii, associated with gliosis and neuronal shrinkage of the internal pallidal segments. These findings give support to the theory, first put forward by Brouwer, that the same principle of systemic degeneration is to be seen in pontoneocerebellar hypoplasia as in olivopontocerebellar atrophy. Some malformations may thus be the early expression of the same abiotrophic process that later reveals itself in the degeneration of certain vulnerable neuronal systems. 19 references. 12 figures.—Author's abstract.

91. *Progressive Cerebral Degenerations of Childhood*. HAROLD STEVENS AND ANATOLE DEKABAN, Washington, D. C. *Neurology* 8:677-681, Sept., 1958.

At present, the onset of progressive deterioration and neurologic defects in a previously healthy child poses a perplexing diagnostic problem. The pediatrician or neurologist is often skeptical of the mother's story that the child was healthy at birth and developed normally. Rather, the conclusion often is erroneously made that a pre-existing birth injury became manifest as the child grew older. A greater awareness that regression due to progressive degenerative disease can occur might increase the frequency with which these conditions are diagnosed and reported, and greater familiarity with the syndromes might motivate more clinicians to pursue the study of the individual case to a finite etiologic diagnosis. The semeiology of this group of defects is more or less uniform. In addition to the history of truncated development or regression and frequently of epileptic attacks, the neurologic examination reveals mental retardation, pyramidal tract signs, and often visual impairment with optic atrophy. Refinement of the diagnosis is dependent largely on laboratory studies. A sequential program of tests is offered, and 5 illustrative cases are presented. Precise diagnosis would permit accumulation of useful data on the diverse mechanisms of progressive cerebral degenerations in childhood. Further, genetic counseling could be offered to the parents in some instances. 9 figures.—Author's abstract.

92. *Akinesia in Parkinson's Disease*. ROBERT S. SCHWAB, ALBERT C. ENGLAND, AND ELIZABETH PETERSON, Boston, Mass. *Neurology* 9:65-72, Jan., 1959.

Both Parkinson and Kinnier Wilson have emphasized the presence of muscular fatigue and lack of endurance in patients with parkinsonism. The authors have developed a special ergograph that records accurately both the voluntary and electrically driven activity of the first dorsal interosseous muscle of the hand. The patient abducts his index finger toward his thumb, pulling a writing pen lever on which there is an adjustable weight. This produces a voluntary ergogram. The electrode from a Batrow stimulator placed over the motor point of this same muscle produces an electronic ergogram that normally is approximately one fifth of the voluntary ergogram because fewer muscle fibers are involved. Some patients with parkinsonism show a better electronic ergogram than voluntary ergogram, although strong motivation can momentarily improve their poor voluntary performance.

Unlike normals and myasthenics, these same patients are not benefitted by rest, as demonstrated when a four second rest is allowed between each movement. The authors have selected the word "akinesia" to include these and other symptoms, such as reduction in level of motor tasks, inability to complete actions, difficulty in releasing muscles, or marked inability to start or sustain one act when another is being done. Subjective complaints include awareness of fatigue in a limb used for repetitive motor acts and a pathologic reduction in the patient's achievement goals. In addition, patients with akinesia show abnormal electroencephalograms and pneumoencephalograms and sensitivity to belladonna and sedative drugs. There is a loss of intellectual ability. Treatment is difficult. Brain surgery is not helpful when the akinesia is severe. Physiotherapy and analeptics are of some value. An understanding family, however, is essential to the proper care and comfort of the patient as the akinesia progresses. 4 references. 5 figures.—Author's abstract.

DISEASES AND INJURIES OF THE SPINAL CORD AND PERIPHERAL NERVES

93. *Arterial Anomalies of the Spinal Cord. Myelographic Diagnosis and Treatment by Section of Dentate Ligaments.* PAUL TENG AND MARVIN J. SHAPIRO, Los Angeles, Calif. A. M. A. Arch. Neurol. & Psychiat. 80:577-586, Nov., 1958.

Arterial anomaly of the spinal cord is not an uncommon disease. It has been frequently misdiagnosed as transverse myelopathy or "degenerative disease of the spinal cord." The misdiagnosis is probably due to nonrecognition of the myelographic findings, which are of various patterns. Because arterial anomalies mainly affect the posterior aspect of the spinal cord, they are better visualized in the supine than in the prone position in myelography. Six cases of arterial anomaly of the spinal cord are discussed. Five patients were treated by laminectomy and resection of the dentate ligaments in the involved segments of the spinal cord. These patients showed satisfactory relief of symptoms. In 3 of them the dentate ligaments of the involved area were noted to be tense and elongated. The section of the dentate ligaments probably relieves "intramedullary tension," caused by both the shrinking cord (atrophy) and the anchorage of the ligaments. This in turn produces relief of symptoms, which are caused primarily by tension or stress and strain rather than by atrophy. In advanced cases, section of the ligaments can hardly be expected to produce any effect on symptoms. Hypothetically, the relief of the intramedullary tension by section of the dentate ligaments may delay the progression of cord atrophy caused by compression, occlusion, or thrombosis of medullary vessels. One patient, treated by laminectomy alone, showed no significant improvement. 10 references. 1 figure. 1 table.—Author's abstract.

94. *Experiences with Metastatic Neoplasms Involving the Spinal Cord.* KEVIN D. BARRON, ASAO HIRANO, SHUKURO ARAKI, AND ROBERT D. TERRY, New York, N. Y. Neurology 9:91-106, Feb., 1959.

In 127 autopsied cases of involvement of the spinal cord and cauda equina by metastatic neoplasms, the most common primary tumors were carcinomas of the lung, breast, and kidney and malignant lymphomas. Sudden onset and rapid progression of symptoms of

cord compression were frequent in these cases and were in striking contrast to the clinical picture usually observed in the primary extramedullary neoplasms of the cord. There were conspicuous differences in the clinical and radiological behavior of metastases from different primary sources. In metastasis from carcinoma of the breast, the following features were almost invariable: (1) A known primary site, (2) a history of pain in the back or pain in a radicular distribution, (3) radiologic evidence of multiple vertebral lesions, and (4) a relatively gradual progression. In contrast, carcinoma of the lung was apt to present as disease of the spinal cord, to be unassociated with pain, to show no vertebral lesions to radiographic examination, and to produce an extremely rapid onset (less than 48 hours) of paraplegia. The clinical behavior of metastasis from carcinoma of the rectum and multiple myeloma resembled carcinoma of the breast, whereas malignant lymphomas and carcinoma of the kidney more closely resembled carcinoma of the lung. Metastases to the thoracic level of the cord were most likely to be associated with fulminant onset and progression. It was noted that lumbar puncture occasionally revealed open manometrics in the presence of paraplegia. Consideration of the myelographic findings suggested that, at least in selected cases, lumbar and cisternal myelography should be combined. In 6 of 38 patients treated surgically, there was striking return of function. Consideration of clinical data indicated that operation was unlikely to be of value when flaccid, areflexic paraplegia was present or when paraplegia had developed in less than 72 hours, when sensory loss was complete, when the primary neoplasm was a carcinoma of the lung. The pathologic changes in the spinal cord were variable, and consistent clinicopathologic correlation was not possible. The gray matter was spared to a large extent, though the white matter was most often affected by an edematous type of malacia distinct from infarction. Intramedullary neoplasms were found in 2 of the 127 patients. 59 references. 7 figures. 5 tables.
—Author's abstract.

ELECTROENCEPHALOGRAPHY

95. *Electroencephalograms of Normal, Full-Term Newborns Immediately After Birth with Observations on Arousal and Visual Evoked Response.* ROBERT J. ELLINGSON, Omaha, Neb. *Electroenceph. & Clin. Neurophysiol.* 10:31-50, Feb., 1958.

Electroencephalograms of 277 normal, full-term babies, aged 20 minutes to 125 hours, were recorded. No relationship was observed between EEG patterns and type of maternal analgesia, type of maternal anesthesia, or length of the second stage of labor. Loud auditory stimuli during sleep may elicit flattening of tracings, K-type response (rare), or both. Spontaneous movement during sleep may also be followed by flattening. Single flash visual stimuli elicit evoked potentials in the occipital area in about half the cases stimulated. These responses differ from those observed in adults in being of more variable wave form, of more variable amplitude, more "fatigable," and of longer latency (160 to 220 milliseconds). Repetitive flash stimuli tend to elicit responses at the beginning and at the end of stimulation (on and off responses). "Driving" effects are rare. The evoked response data are interpreted as reflecting the physiological immaturity, associated with the known anatomical immaturity, of the brain of the newborn. 60 references. 11 figures. 2 tables.
—Author's abstract.

96. *The Persistence of the Juvenile Electroencephalogram.* GOTTFRIED ROTH, Vienna, Austria. Psychiat. et Neurol. 136:195-203, Oct.-Nov., 1958.

The human electroencephalogram shows a maturation parallel to the development of the individual. An inhibition of maturation may be observed both clinically and bioelectrically. In routine studies, a large number of patients more than 20 years of age showed an occipital alpha rhythm, which may generally be seen in persons between 10 and 13 years of age. A catamnestic review of clinical histories of patients with a persistent juvenile electroencephalogram revealed that in a majority of cases the diagnosis denoted neurotic syndromes (psychoneuroses or organic neuroses). The persistent juvenile EEG must first be related to the ontogenetic maturation process. These findings indicate the possibility of bioelectrical confirmation of clinical and constitutional infantilism or psycho-infantilism, with retardation as an explanatory principle. 17 references.—Author's abstract.

97. *Cortical and Subcortical Electrical Effects of Psychopharmacologic and Tremor-Producing Compounds.* W. W. KELBER AND R. E. CORRELL, Iowa City, Iowa. A. M. A. Arch. Neurol. & Psychiat. 80:544-553, Nov., 1958.

The administration of chlorpromazine was invariably followed by the appearance of slow activity of increasing voltage that was very similar to that of natural sleep. This change was not seen following administration of reserpine. Of the subcortical structures studied, the intralaminar nuclei of the thalamus showed the greatest response to chlorpromazine and the hippocampus the least. The globus pallidus showed less slowing under chlorpromazine than during natural sleep. Within the limits of testing, chlorpromazine had little effect on the electrical response to sensory stimulation. Seizure-like activity sometimes followed the administration of either chlorpromazine or reserpine but was more frequently seen after the latter. The cortical and subcortical electrical effects of four compounds, chlorpromazine, reserpine, Tremarine, and pentobarbital, each capable of producing tremor under various conditions, showed very little resemblance to one another. Potentiation of cortical fast activity normally produced by Tremarine, when pentobarbital was added to the same preparation, correlated to a fairly high degree with the persistence and amplitude of the tremor. Conversely, the "competitive" effects of chlorpromazine and Tremarine in combination frequently were manifested by subsidence of the tremor. Results to date do not support the conclusion that activation of the midbrain reticular formation may be evoked as the mechanisms of chlorpromazine or reserpine tremor. 17 references. 6 figures.—Author's abstract.

HEAD INJURIES

98. *Persistent Psychiatric Disorders After Head Injuries in Children.* J. A. HARRINGTON AND F. J. J. LETEMENDIA, Birmingham, England. J. Ment. Sc. 104:1205-1218, Oct., 1958.

This study was undertaken to investigate the long-term psychiatric sequelae of head injuries in children. Thirty-one children with head injuries attending a child psychiatric clinic were compared with 32 children of similar age who had been admitted with head

injuries to a surgical ward some years previously. The children from the surgical ward had sustained more severe head injuries, as judged by the presence of skull fracture, duration of unconsciousness, and neurologic sequelae, but, as had been predicted, they showed far less psychiatric disorder than those examined at the child psychiatric clinic. A wide variety of symptoms was encountered, but few appeared to be specific or causally related to the head injuries. The fracture site had no clear relationship to subsequent behavior disorder. The pretraumatic personality and family setting were far more important for the psychiatric outcome than the nature and severity of the head injury. A generally favorable outcome even after severe head injury in previously well-adjusted children was confirmed, but where children showed evidence of marked emotional disturbance before the accident, the outcome was far less favorable and was dependent on the persistence of adverse factors at home. The families of children who showed chronic posttraumatic disorders showed a high incidence of psychiatric disturbances. Accident proneness was twice as frequent in the psychiatric clinic cases, and there was evidence that this was related to emotional disorder. In the management of the psychiatrically disturbed cases the educational aspects were found to be of primary importance; in these cases full psychological investigation and special remedial teaching was an important aspect of treatment. 15 references. 5 tables.—Author's abstract.

INFECTIOUS AND TOXIC DISEASES OF THE NERVOUS SYSTEM

99. *Influenza Encephalopathy and Postinfluenza Encephalitis.* T. H. FLEWETT AND J. G. HOULT, Birmingham, England. Lancet 2:11-15, July 5, 1958.

Cases are described of neurological illness associated with Asian-type influenza infection. These fall into four groups. In group 1 the association of influenza with clinical encephalitis is quite clear, since Asian-type virus was isolated from the lungs of 6 fatal cases showing a congested brain at necropsy. The relationship of influenza infection to encephalitis or to ascending paralysis of Guillain-Barré type in patients in groups 2 and 3 is less clear, since no virus was isolated although positive serological tests for influenza were obtained. On the other hand, positive serological tests were common in the population at the time, when the epidemic was at its height. In group 4, tests for influenza virus infection were negative in 6 patients with a history of an influenza-like illness followed by neurological illness. An attempt is made to assess the significance of positive serological findings for influenza in cases of encephalitis at a time of epidemic spread. It is concluded that more evidence is needed before the etiological relationship between influenza virus infection and postinfluenza encephalitis can be accepted. 17 references.—Author's abstract.

TREATMENT

100. *Dystonia Musculorum Deformans Alleviated by Chemopallidectomy and Chemopallidothalamectomy,* IRVING S. COOPER, New York, N. Y. A. M. A. Arch. Neurol. & Psychiat. 81:5-19, Jan., 1959.

Dystonia musculorum deformans, which has previously been demonstrated to be a pro-

gressive incapacitating disease of childhood characterized by involuntary movements and deformities, has heretofore been considered to be unresponsive to medical, surgical, physical, or psychiatric therapy. This investigation demonstrates that dystonia musculorum deformans in children can be alleviated by sufficiently large, accurately placed lesions in the globus pallidus and/or ventrolateral nucleus of the thalamus. During the course of this investigation, 16 children with advanced dystonia musculorum deformans were subjected to chemopallidectomy and/or chemothalamectomy. In 3 patients operation was carried out bilaterally. Thirteen of these 16 patients demonstrated marked alleviation and reversal of the involuntary movements and deformities of this disease. Such relief has now persisted for more than two years in several of these children. The disease entity of dystonia musculorum deformans can no longer be considered as a hopeless, irreversible disease. The treatment of choice of dystonia musculorum deformans is chemopallidectomy and/or chemothalamectomy. 12 references. 10 figures.—Author's abstract.

BOOK REVIEWS

Multivariate Correlational Analysis. PHILIP H. DUBOIS. New York. Harper and Brothers, 1957. 202 pp. \$4.50.

The author relates Yule's methods of dealing with multiple and partial correlation to the matrix methods in common use and presents a matrix method for which he discusses the statistical meaning of the elements at each stage of analysis. Computing routines and checking methods are provided. The relationship of multiple and partial correlation to factor analysis and the implications of multivariate analysis for social science research are discussed. The book presupposes acquaintance only with the Pearson product-moment correlation coefficient, and can therefore be used by students in elementary statistics. It will be of little interest to students beyond that level, since there is little stress on underlying assumptions and the mathematical treatment is superficial.—Margaret Mercer, Ph.D.

The Doctor Eyes the Poor Reader. DELWYN G. SCHUBERT. Springfield, Ill. Charles C Thomas, 1957. 101 pp. \$3.75.

This short book furnishes a good deal of useful information. It is written primarily for the general practitioner but could also be helpful to optometrists, educators, psychologists, and interested parents. The author emphasizes the fact that reading disability is a complex problem with many possible causes, such as visual, auditory, and speech defects, other physical factors, including poor general health, glandular dysfunction, sex differences, and neurological and dominance difficulties, emotional maladjustment, intellectual retardation, educational inadequacies, and poor home environment. Although one factor may be more important than another in any individual case, more than one factor is usually involved. A chapter is devoted to the diagnosis and treatment of the visual problems that may influence reading ability, and there are shorter discussions of other factors. The author presents objective symptoms and outlines screening tests both with and without instruments. He familiarizes the doctor with some of the methods and approaches used by teachers and specialists in diagnosing reading problems and instructing poor readers.

He also includes a letter that doctors may reproduce giving specific suggestions to the parents of poor readers. There is even a chapter designed to show the doctor and other readers how to improve their own reading skills. Although this book does not contribute any new ideas on reading disability, it provides a clear and concise review of the principal aspects of the problem.—*Claudene Seidel, A.M.*

The Person in Psychology: Reality or Abstraction. PAUL LAFITTE. New York. Philosophical Library, 1957. 233 pp. \$6.00.

This volume is concerned with the nature and limitations of psychology. Marshaling supportive views from phenomenological and self-psychologists, existential philosophers, semanticists, and logicians, the author defines psychology in terms of the study of the common experiences of the person. With emphasis on common experience and on the individual as a continuously perceiving and evaluating person, he questions the relevance to psychology of: (1) Physiological studies whose results are dependent upon physical factors, (2) animal laboratory experiments from which there is very limited transfer of knowledge to the human level, (3) the special languages of psychoanalysis and other schools of psychology, which constitute a regrettable barrier to communication among psychologists, and (4) the use of parametric statistics whose abstractions demand diligent and critical analytical interpretation as well as additional interpretation in relation to a specific person's life experiences. The author's conclusion is that psychologists must study the person as an agent of his becoming, a cause of his behavior, not merely as an object. He then turns to methods of psychology. He states that, in dealing with the practical problems of psychological inquiry, the psychologist is concerned with economy of effort, relevance of data, and kinds of hypothesis to be derived. Attention is focused on the nature of the data to be obtained, on the methods for obtaining data, and, generally, on the degree of abstraction implicit in the original data and the reduction of data to some kind of orderly system.

The subsequent meaning of scientific inquiries can be enhanced to the degree that the psychologist is aware of the following processes in the planning and in the subsequent treatment of data: (1) Substantial abstraction, or the choice of general area and level of recurrent behavior to be studied, (2) instrumental definition, or the initial degree of definition of items in terms of range, order, and freedom of response, (3) categorical abstraction, or the classification of items into variables, categories, and distributions, and, after the inquiry proper, (4) synthetic abstraction, or the classification of the raw data according to theoretical formulations and/or statistical aggregations. The methods of psychological inquiry are then examined in the light of these abstracting processes. Each method is evaluated in relation to the precision, economy, relevance, and strength of hypotheses derived with respect to the legitimate abstractions that naturally take place within each method. The psychologist's general concern at all times should be with his ability to demonstrate the relation between his final abstractions and the common, recurrent behavior of the person. When such attention is given to the individual as a causal agent in terms of his own life experiences, a coherent, disciplined psychology of the person will develop.

This book is a searching analysis of the substance and nature of psychology. It is easy to appreciate the philosophical argument for focusing attention on the person. On the

other hand, the discussion of the problems of psychological inquiry requires considerable thought. When the author discusses the methods of psychology in relation to the various degrees of abstraction involved, he is concerned with reliability and validity, the confidence with which the psychologist can apply his generalizations to a person. In short, he argues for simplification, systematization, and intensification of psychological inquiries.—Arnold O. D. Peterson, Ph.D.

Hamlet's Mousetrap. ARTHUR WORMHOUDT. New York, N. Y. Philosophical Library, Inc., 1958. 220 pp. \$3.50.

The author is a professor of English at a state teachers' college. The book is an attempt to explain literary form, grouping of words, and grammatical structure in terms of psychodynamics, expressed in psychoanalytic formulations, that are operative in the development of the literary ability of an author. Dr. Wormhoudt relies heavily on the work of the psychoanalyst, Eugene Berger, who has evolved a psychoanalytic interpretation of literary productivity and inhibition in terms of unconscious conflicts and the defenses against them.

Approximately the first third of the book is a presentation of the psychoanalytic theory pertinent to the thesis that the form of a piece of literature is closely tied up with the unconscious psychodynamics of its author. Greatest emphasis is placed on the conflicts centered around the oral needs of the infant. Because of the infant's complete helplessness he is unable to obtain food immediately when he is hungry, so that he must inhibit his needs, and he does this by hallucinations, at first of touch sensations, later smell, vision, and hearing. This substitutive type of gratification causes a reproach of conscience that the infant wants to deny himself food. As a defense against this accusation of conscience, speech becomes equated with liquids, and speech and words then are used as a kind of ruse to deny the reproach of conscience that the individual wishes to be denied food, and thus conscience becomes somewhat appeased. It is Dr. Wormhoudt's proposition that the vicissitudes and dynamic operations of these oral conflicts and their subsequent elaboration by a process of projection and identification can be followed in the literary creation of the individual author, and that they determine the form and structure of the literary production used by the author.

The second portion of the book, which comprises about two thirds of it, is an application of the psychoanalytic formulation presented in the first third of the book to Shakespeare's Hamlet. He does this act by act and scene by scene, showing how the literary form, the appearance of the characters, and the characters themselves are determined by unconscious conflicts in the author centered about oral needs.

The application of psychoanalytic concepts in attempting to understand how psychodynamics determines the structure and the organization of a literary production is certainly a stimulating and new approach to the study of literature. Most psychoanalytic studies in the past have confined themselves simply to the content rather than to the actual grammatical structure and form of a composition. The main criticism is the author's unwarranted elaboration of basic psychoanalytic theory. This is done arbitrarily, without the inclusion of any empirical material to justify and substantiate such elaboration. One gets the impression that this extension of psychoanalytic theory was obtained from the same source that was used for substantiating or validating it, namely, Shakespeare, so that a

type of circular reasoning seems to be operating. Many of his theoretical formulations are expressed in such abstract terms that they are hard to follow, and even harder to apply intelligibly to actual literary material. The reviewer does not believe that Dr. Wormhoudt's book has been particularly helpful either in furthering the understanding of literary form or of extending psychoanalytic theory; however, the book is successful in presenting a new approach and in creating an interest in further study and in elaboration of this approach as a method of study of the literary form.—*Arthur H. Kiracofe, M.D.*

Reaching Delinquents Through Reading. MELVIN ROMAN. Springfield, Ill. Charles C Thomas, 1957. 125 pp. \$4.50.

This book examines the effectiveness of what the author calls tutorial group therapy (psychotherapy in a group setting directed toward simultaneous correction of reading disabilities and improvement of mental health) in facilitating psychosocial adjustment and correcting reading retardation. The author compares tutorial group therapy with group remedial reading and interview group therapy, presenting statistical material to support the thesis that this therapy is superior to either of the other methods. His subjects were 21 delinquent boys on active status in the treatment clinic of the Manhattan Children's Court in New York, ranging in age from 13 to 16 years of age, and divided into three groups of 7 each. He feels that a large percentage of delinquent children have reading disabilities, that their reading difficulties are really an organic problem, and that one must deal with the total personality.—*Irving L. Berman, M.D.*

Ten Million and One. ALICE FITZ GERALD AND JUSTIS J. SCHIFFERES (editors). New York. Harper (Hoeber), 1957. 102 pp. \$3.50.

This is a compilation of observations, opinions, and recommendations of several authorities in the field of neurological diseases, particularly as they relate to public relations, socio-economic consequences, and the multidisciplinary problem of research and rehabilitation. It is a report on the conference on neurological disability as a national problem, sponsored by The National Health Council. It is estimated that there are about 10 million victims of neurological disease in this country. It is emphasized that: (1) Direct and indirect cost of neurological disease is staggering, (2) there is need for compilation of precise statistics on the incidence of neurological disorders and for expansion of facilities for care and treatment of the neurologically disabled, with emphasis on rehabilitation, (3) there is a lack of trained personnel to participate in epidemiologic studies, clinical and laboratory research, and diagnosis and treatment, and (4) education of lay groups and physicians must be planned. Problems in the philosophy of programming research in neurological disease are presented and future needs outlined.—*Harold Stevens, M.D.*

The Infantile Cerebral Palsies. E. COLLIS, W. COLLIS, W. DUNHAM, L. HILLIARD, AND D. LAWSON. Springfield, Ill. Charles C Thomas, 1957. 100 pp. \$3.00.

Cerebral palsy, a potpourri of disorders of movement, is primarily a problem in child neurology. Varieties of disciplines converge particularly on the physiology of movement

to give shape and substance to the generic term cerebral palsy. Excerpts from Little's original work in 1853 are presented, and a brief biographical sketch of his life is given. The principal types of cerebral palsy are identified and described (infantile cerebral palsy, generalized spasticity, hemiplegia, variable rigidity, athetoid cerebral palsy, and ataxic cerebral palsy). The diagnosis and management of each type is outlined, and typical cases are cited, with emphasis on early recognition and attempts to educate the child for maximum utilization of his limited resources. Continuity of treatment is vital, and parental participation is essential. The book is primarily for the layman interested in cerebral palsy.—*Harold Stevens, M.D.*

Deafness, Mutism, and Mental Deficiency in Children. LOUIS MINSKI. New York. Philosophical Library, 1957. 82 pp. \$3.75.

This book sets forth the experience of the author in the diagnosis and treatment of children who lack hearing or show an absence of speech. The problem is a difficult one, has a devastating impact on the family, and challenges the clinician and educator. Since successful treatment is dependent upon early diagnosis and the application of appropriate methods of training, it is important for the pediatrician, child psychiatrist, psychologist, and educator to be able to discern the problem. The general aspects are discussed with regard to early detection, the development of normal speech, deviation in communication, and the psychological disturbances that are frequently seen in these children. The impact on the family may extend from frank rejection to overprotection and intensify the problems of the child. Differential diagnosis of deafness and mutism, either congenital or acquired, must be made in relation to mental deficiency, hysteria, autism, schizophrenia, and speech that is psychologically delayed. Most commonly the diagnosis rests between a form of deafness on an organic basis and mental deficiency. The causes of hearing and speech defect, congenital and acquired, are reviewed. The staffing of inpatient and clinic units are discussed. The inpatient service is for children who are observed for a longer period of time to clarify the nature of the disorder and to correct concurrent psychological problems. The importance of an excellent developmental history is stressed and general methods of assessment of the educability of the child described. The more specific tests are briefly listed including audiometry, electrophysiological methods of assessment, and the psychological tests, especially the Merrill-Palmer and the Drever-Collins tests.

The reviewer feels that more on the impact of such disturbed children upon the parents and treatment of the emotional disturbance in the family should have been included, as well as more information about the significance of the psychological tests and more data on the treatment methods and sources of reference material. However, the book is of value to pediatric and psychiatric clinics, the pediatrician, child psychiatrist, and the educator at the nursery school and primary school levels.—*Sidney Berman, M.D.*

Live and Let Live—The Moral of the Wolfenden Report. EUSTACE CHESSER. New York. Philosophical Library, 1958. 124 pp. \$4.75.

It is perhaps too much to expect subjects such as homosexuality and prostitution to be dealt with objectively and rationally, at least in this country. It is heartening, however, to

record a good start made in England in the form of the Report of the Departmental Committee on Homosexual Offences and Prostitution, better known as the Wolfenden Report. The present volume is an attempt to outline the report, and to comment on its rationale. Briefly, the report distinguishes between crime and sin, and in general adopts the attitude that sexual relations between consenting adults, be they of the same or opposite sex, if carried on in private, are of no proper public concern as criminal. Both the Moral Welfare Council of the Church of England and the Roman Catholic Advisory Committee appointed by the late Cardinal Griffin agreed on this point, namely, that "the duty of the State is not to intervene in the purely private sphere, but to act solely as the defender of the common good." The author debunks some of the muddled thinking on the subject of sex, with particular reference to the two main topics of the report. The book should be read widely; it might even modify a few prejudices! —Winfred Overholser, M.D.

Books Received for Review

The World of Dreams. HENRI BERGSON. New York. Philosophical Library, 1958. 58 pp. \$2.75.

Group Psychoanalysis. B. BOHDAN WASELL. New York. Philosophical Library, 1959. 306 pp. \$3.75.

Readings in Psychoanalytic Psychology. MORTON LEVITT, editor. New York. Appleton-Century-Crofts, 1959. 413 pp. \$8.50.

Psychopharmacology—Problems in Evaluation. JONATHAN O. COLE AND RALPH W. GERARD, editors. Washington, D. C. National Academy of Sciences and National Research Council, 1959. 662 pp. \$6.50.

Child and Juvenile Delinquency. BENJAMIN KARPMAN. Washington, D. C. Psychodynamics Monograph Series, 1959. 364 pp. \$10.00.

Group Processes—Transactions of the Fourth Conference, 1957. BERTRAM SCHAFFNER, editor. New York. Josiah Macy Jr. Foundation, 1959. 266 pp. \$4.50.

Essentials of Clinical Neuroanatomy and Neurophysiology. JOHN T. MANTER. Philadelphia. F. A. Davis Co., 1958. 137 pp. \$3.00.

Thrills and Regressions. MICHAEL BALINT. New York. International Universities Press, 1959. 148 pp. \$4.00.

Mannerisms of Speech and Gestures in Everyday Life. SANDOR S. FELDMAN. International Universities Press, 1959. 301 pp. \$5.00.

The Unconscious in History. A. BRONSON FELDMAN. New York. Philosophical Library, 1959. 269 pp. \$4.75.

The Clinical Examination of Patients with Organic Cerebral Disease. R. KLEIN AND W. MAYER-GROSS. Springfield, Ill. Charles C Thomas, 1959. 95 pp. \$3.50.

Collected Papers of Sigmund Freud. ANNA FREUD, ERNEST JONES, JOAN RIVIERE, ALIX STRACHEY, AND JAMES STRACHEY, editors. Translated by JAMES STRACHEY. Basic Books, 1959. 5 volumes, boxed. \$25.00.

Breakdown. ROBERT DAHL. Indianapolis, Ind. Bobbs-Merrill Co., 1959. 288 pp. \$3.95.

Man's Right to be Human. GEORGE CHRISTIAN ANDERSON. New York. William Morrow & Co., 1959. 191 pp. \$3.50.